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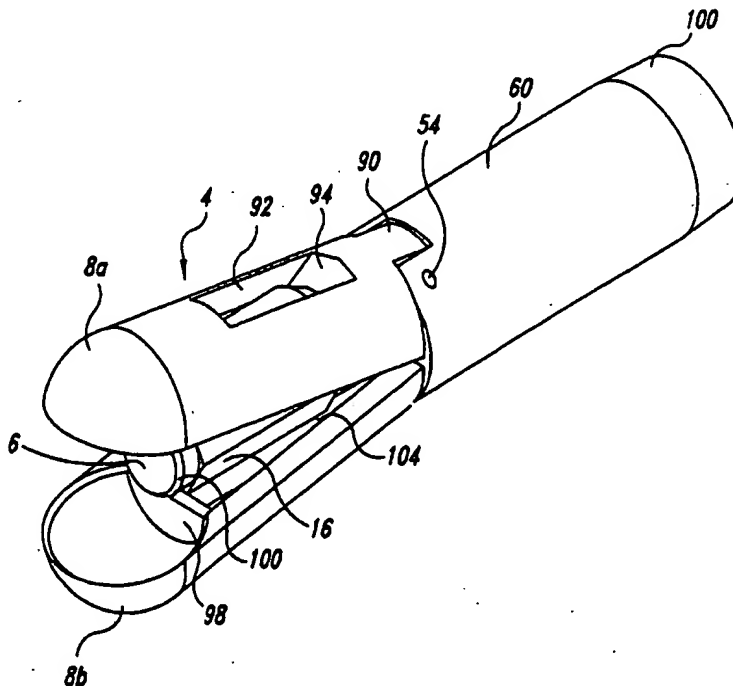
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(54) Title: CATHETERS AND ENDOSCOPES COMPRISING OPTICAL PROBES AND BIOPTOMES AND METHODS OF USING THE SAME

(57) Abstract

Apparatus and methods relating to an optical bioptome disposed at the distal end of a catheter or endoscope. The optical bioptome comprises an optical probe that is preferably extensible and retractable axially along the length of the catheter or endoscope, and the jaws of the optical bioptome are opened when the optical probe is extended and the jaws are closed when the optical probe is retracted.



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CATHETERS AND ENDOSCOPES COMPRISING OPTICAL PROBES AND BIOPTOMES AND METHODS OF USING THE SAME

CROSS-REFERENCE TO RELATED APPLICATIONS

This application claims priority from United States provisional patent
5 application No. 60/040,557, filed March 13, 1997, United States provisional patent
application No. 60/046,368, filed May 15, 1997, and United States provisional patent
application No. 60/053,688, filed July 25, 1997, all of which are presently pending.

TECHNICAL FIELD OF THE INVENTION

The present invention relates to catheters and endoscopes for optical
10 scanning or analysis, the catheters and endoscopes comprising biptomes comprising
opposed jaws, push rods that open and close the jaws, and/or optical probes.

BACKGROUND OF THE INVENTION

A standard method for conducting analysis of tissue *in vivo* is the
conduction of physical, or tissue, biopsies. For example, in the case of heart
15 transplants, accurate diagnosis of the presence or absence of rejection is vital for the
effective care of the heart transplant, and percutaneous transvenous endomyocardial
biopsy (EMB) is a standard method for such assessment of rejection. Crudely
described, this means inserting a catheter comprising a biptome, which comprises a
wire with tiny jaws at the distal end, into a blood vessel. Many varieties of catheters
20 and biptomes are known in the art. *See, e.g.*, U.S. Patent No. 3,964,468; U.S. Patent
No. 4,953,559; U.S. Patent No. 4,884,567; U.S. Patent No. 5,287,857; U.S. Patent
No. 5,406,959; WO 96/35374; WO 96/35382; WO 96/29936; WO 96/35374. The distal
end of the catheter is fed into an entry point, typically on the leg or neck, and then on to
the heart chamber where a tiny piece of tissue is clamped in the jaws of the biptome
25 and removed for analysis. This biopsy permits accurate detection of the presence and
the severity of histologic changes in the transplanted tissue once the site of rejection is
found.

A typical schedule for EMBs is as follows:

Table 1

Right Ventricular Biopsy Protocol for Heart Transplant			
Period	Time	Frequency	Procedures
Immediate post-operative	0-4 weeks	from day five, twice weekly	6
	4-6 weeks	weekly	3
Late post-operative	2-3 months	bimonthly	4
	4-6 months	monthly	3
	6-12 months	quarterly	2
Total	First Year		18
	After one year	yearly (in the absence of rejection)	
After rejection therapy		14-21 days	

5

A patient requires an average of 5, and may require as many as 10, biopsies per biopsy procedure. Thus, over the first year of a heart transplant recipient, as many as 180 EMBs are taken.

The heart material obtained from the biopsy is then graded for the level or severity of the rejection.

EMBs, and other biopsies, are problematic, however, because during each biopsy a number of potential complications may occur. These complications include the following:

- right ventricular perforation
- cardiac tamponade
- ventricular and supraventricular arrhythmia
- embolus (thrombus or air)

15

pneumothorax air in the pleural cavity

infection

bleeding

Thus, tissue biopsy is hazardous for the patient, but a patient may have to
5 undergo more than 100 tissue biopsies subsequent to a major procedure such as an
organ transplant. Attempts have been made to reduce the number of biopsies per
patient, but these attempts have not resolved the difficulty in pinpointing the sites where
biopsy is needed nor the difficulty in assessing tissue without performing the actual
biopsy.

10 Accordingly, there has gone unmet a need for apparatus and methods
that reduce the number of biopsies that a patient must suffer. There has also gone
unmet a need for methods and devices that assist in pinpointing sites where rejection
starts. The present invention provides these and other related advantages.

SUMMARY OF THE INVENTION

15 The present invention provides apparatus and methods for analyzing a
target tissue to determine whether the tissue needs to be biopsied, and for obtaining a
biopsy if it is found to be needed. Generally, the apparatus comprise an optical
bioptome disposed at the distal end of a catheter or endoscope. The optical bioptome
comprises an optical probe that is preferably extensible and retractable axially along the
20 catheter or endoscope, and preferably the jaws of the optical bioptome are opened when
the optical probe is extended and the jaws are closed when the optical probe is retracted.

Accordingly, the present invention provides catheters and endoscopes
comprising a bioptome comprising one or more opposed jaws and an extensible and
retractable optical probe that extends distally and retracts proximally, wherein the jaws
25 are open when the optical probe is extended and the jaws are closed when the optical
probe is retracted. Preferably, the optical probe is disposed between the jaws.

In another aspect, the present invention provides a catheter or endoscope
comprising a bioptome comprising opposed jaws that are maintained in a closed
position, for example by spring loading or by contact with the optical probe. One or

more of the jaws comprise a central body, a distal scoop and an internal proximal surface, the catheter further comprising a push rod that extends distally and retracts proximally along a path disposed between the jaws, wherein the central body of the at least one jaw comprises a projection that projects into the path of the push rod such that

5 the push rod contacts the projection as the push rod extends distally thereby forcing the jaws apart. And, when the push rod is retracted in a proximal direction, the push rod separates from the projection and a proximal shoulder of the push rod contacts the internal proximal surface of the jaw, thereby causing the jaws to close, preferably because the jaw is shaped such that the internal surface projects into the path of the push

10 rod, for example from a hinge, and the contact causes the jaw to rotate or bend inwardly about the hinge to close the jaws. In another preferred embodiment, the proximal shoulder of the push rod extends radially outward from the push rod at a first acute angle with respect to a displacement axis of the push rod, and the internal proximal surface of the jaw extends radially inward with respect to the displacement axis of the

15 push rod at a second acute angle. The first acute angle and the second acute angle are preferably about the same. When the proximal shoulder and the internal proximal surface contact one another during proximal retraction of the push rod relative to the jaw, the proximal shoulder forms an overhang over at least a portion of the internal proximal surface of the jaw.

20 Preferably, the projection is a thickened portion of the jaw that tapers in thickness in a proximal direction, such that the thickness of the thickened portion is greater at a distal end of the thickened portion than at a proximal end of the thickened portion. Also preferably, the push rod tapers in thickness in a distal direction at an impact surface of the push rod that contacts the thickened portion of the central body of

25 the jaw, such that the thickness of the push rod is lesser at a distal end of the impact surface than at a proximal end of the impact surface. Further preferably, both the jaw and the push rod comprise such tapers.

In one preferred embodiment, the optical probe comprises at least one illumination light guide suitable for conducting light from a proximal end to a distal end

30 of the catheter and for emitting the light from a distal end of the illumination light guide

and at least one collection light guide suitable for collecting light entering a distal end of the collection light guide and conducting the light to the proximal end of the catheter. The illumination light guide and the collection light guide can be a single optic fiber. In another preferred embodiment, the optical probe comprises at least three collection light
5 guides that are equally radially disposed around the at least one illumination light guide, or the optical probe comprises at least three pairs of light guides, each pair comprising at least one of the illumination light guide and the collection light guide, and wherein the distance from the collection light guide to the illumination light guide is equal in each of the at least three pairs.

10 In another preferred embodiment, the optical probe comprises an image sensor and one or more light guides to transmit an image gathered by the image sensor from the distal end of the catheter or endoscope to the proximal end of the catheter or endoscope.

In another aspect, the present invention provides a method for
15 determining whether a target tissue exhibits one or more characteristics indicating that the target tissue be biopsied, the method comprising: placing the opposed jaws of the catheters or endoscopes of the present invention adjacent to a target tissue *in vivo*; extending the optical probe and opening the jaws of the catheter; emitting light from the distal end of the catheter or endoscope under conditions suitable to cause light to
20 emanate from the target tissue, to provide emanating light; collecting the emanating light; and, evaluating the emanating light to determine whether the target tissue exhibits one or more characteristics indicating that the target tissue be biopsied.

In a further aspect, the present invention provides a method for determining the orientation of an optical probe relative to a target tissue, the method
25 comprising: placing the opposed jaws of the catheter described herein having at least three collection light guides disposed radially about an illumination light guide adjacent to a target tissue *in vivo*; extending the optical probe and opening the jaws of the catheter; emitting light from the at least one illumination light guide to the target tissue under conditions suitable to cause light to emanate from the target tissue, to provide
30 emanating light; collecting the emanating light entering the at least three collection light

guides; measuring the relative intensity of the light collected by each of the at least three collection light guides; and, therefrom determining an orientation of the optical probe with respect to the target tissue.

In a functionally related method using the catheters described herein
5 comprising at least three pairs of illumination and collection light guides, after placing the opposed jaws of the catheter adjacent to the target tissue, extending the optical probe and opening the jaws of the catheter, light is emitted from each of the at least three illumination light guides to the target tissue under conditions to cause light to emanate from the target tissue, to provide emanating light, then the emanating light is
10 collected entering the at least three collection light guides. The relative intensity of the light collected by each of the at least three collection light guides is measured, and therefrom the orientation of the optical probe with respect to the target tissue is determined.

Preferably, after the orientation of the optical probe is determined, the
15 methods further comprise determining whether the orientation of the optical probe is adequate to provide data sufficient to indicate that the target tissue exhibits one or more characteristics indicating that the target tissue be biopsied. Also preferably, if a biopsy is indicated, the methods further comprise obtaining the biopsy by retracting the optical probe and closing the jaws of the catheter, thereby removing a piece of the target tissue
20 from the target tissue.

These and other aspects of the present invention are discussed further in the following Detailed Description and the attached drawings. In addition, various references are set forth herein that describe in more detail certain procedures or apparatus, etc. (e.g., bioptomes, optical probes, etc.); all such references are
25 incorporated herein by reference in their entirety.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 is an isometric view of one embodiment of an optical bioptome according to the present invention.

Figure 2 is a first side view of the optical bioptome depicted in Figure 1.

Figure 3 is an isometric view of the optical bioptome of Figure 1 when the jaws are in a closed position.

Figure 4 is a second side view of the optical bioptome of Figure 1.

Figure 5 is an exploded isometric view of the optical bioptome of
5 Figure 1.

Figure 6 is a side view of a second embodiment of an optical bioptome according to the present invention with the jaws slightly open.

Figure 7 is an isometric view of the optical bioptome depicted in
Figure 6.

Figure 8 is a cross-sectional side view of the optical bioptome depicted
10 in Figure 6.

Figure 9 is a first side view of the optical bioptome depicted in Figure 6.

Figure 10 is a second side view of the optical bioptome depicted in
Figure 6.

Figure 11 is an exploded isometric view of the optical bioptome depicted
15 in Figure 6.

Figure 12 is an isometric view of the bioptome detached from the catheter body, in a modular format.

Figure 13 is an isometric view of a third embodiment of an optical
20 bioptome according to the present invention with the jaws slightly open and detached from the catheter body, in a modular format.

Figure 14 is a side view of the optical bioptome depicted in Figure 13.

Figure 15 is a cross-sectional side view of a jaw of the optical bioptome
depicted in Figure 13.

Figure 16 is a bottom plan view of the jaw depicted in Figure 15.
25

Figure 17 is a top plan of a push rod of the optical bioptome depicted in
Figure 13.

Figure 18 is a side view of the push rod depicted in Figure 17.

Figure 19 is an isometric view of the push rod depicted in Figure 17.

Figure 20 is a side view of an optical bioptome comprising only a single rotatable jaw.

Figure 21 depicts an exploded, cross-sectional side view of a optical bioptome as set forth herein designed to be threaded into the tip of the catheter or
5 endoscope.

Figure 22 depicts an exploded, cross-sectional side view of a catheter described herein, wherein the bioptome and the push rod for the optical probe are threaded onto the tip of the catheter and sheath of the optical probe, respectively.

Figure 23 depicts an exploded isometric view of the optical bioptome
10 depicted in Figure 22.

Figure 24 depicts a cross-sectional side view of the optical bioptome of Figure 22.

Figure 25 depicts a cross-sectional side view of an optical bioptome wherein the jaws are spring-loaded to be biased against one another.

Figure 26 depicts an exploded cross-sectional side view of the optical bioptome of Figure 25.

Figure 27 depicts a generalized view of a catheter or endoscope of the present invention including the proximal end thereof, and wherein the optical probe is maintained in side-by-side relation with the bioptome.

Figure 28 depicts a side view of a scissors-like control and actuation device suitable for use with a catheter or endoscope of the present innovation.

DETAILED DESCRIPTION OF THE INVENTION

The present invention provides endoscopes, catheters and methods for optically analyzing a target tissue to determine whether the tissue needs to be biopsied,
25 and to remove a biopsy of the tissue without withdrawing the endoscope or catheter between obtaining the optical analysis and obtaining the tissue biopsy. Generally, the apparatus comprises an optical bioptome disposed at the distal end of the catheter or endoscope. Typically, the optical bioptome includes an optical probe that is extensible and retractable along the catheter or endoscope such that the optical probe is disposed

between the jaws of the bioptome when the jaws are open, and the optical probe is retracted when the jaws are closed.

Thus, the optical bioptome of the present invention allows optical assessment of tissue to assist the surgeon in both selecting optical scanning sites and in performing biopsy, and thus allows simple and easy biopsy with minimal risk and reduced harm to the patient because of shortened overall surgical procedure time and fewer insertions of catheters and endoscopes into the body. These advantages are achieved because fewer tissue biopsies should be necessary because no biopsy will be taken when the optical scan shows that there is no need for biopsy, and because the combination of the bioptome with the optical probe permits optical scanning and biopsy without removal of the catheter or endoscope carrying the optical bioptome.

An "optical bioptome" is an apparatus that comprises an optical measurement/imaging device, or probe, and a tissue biopsy device, or bioptome, and is typically located at the distal end of a catheter or endoscope. As noted above, a bioptome is a device that snips off a piece of a target tissue for extraction from an organism and evaluation. Bioptomes typically comprise a pair of opposing jaws, but other configurations are also known. U.S. Patent No. 3,964,468; U.S. Patent No. 4,953,559; U.S. Patent No. 4,884,567; U.S. Patent No. 5,287,857; U.S. Patent No. 5,406,959; WO 96/35374; WO 96/35382; WO 96/29936; WO 96/35374. Optical probes and methods of analyzing scans using the same are also well known in the art. U.S. Patent No. 5,421,337; U.S. Patent No. 5,507,287; U.S. Patent No. 5,467,767; U.S. Patent No. 5,071,416; U.S. Patent No. 5,042,494; U.S. Patent No. 5,062,428; U.S. Patent No. 4,836,203; U.S. Patent No. 4,845,552; EP 0/595,506; WO 95/26673.

As is well known in the art, insertion elements, such as catheters and endoscopes, are generally tubular devices for insertion into a body, typically via canals, vessels, passageways or body cavities for any of a variety reasons, including diagnostic purposes such as those described herein as well as other purposes such as the injection or withdrawal of fluids or to keep a passageway open. The distal end of a catheter or endoscope is the end of the catheter or endoscope that is inserted into the body and directed to a target tissue; the proximal end is the end of the catheter or endoscope that

is maintained outside the body, and typically comprises a one or more handles, knobs and/or other control devices that allow the user to manipulate the distal end of the catheter or endoscope and/or devices located at the distal end of the catheter or endoscope. As used herein, the distal end of the catheter or endoscope includes the distal tip of the catheter or endoscope, which is the most distal surface or opening of the catheter or endoscope and the portion of the catheter or endoscope adjacent to the distal tip of the catheter. Catheters and endoscopes are generally well known. U.S. Patent No. 5,409,000; U.S. Patent No. 5,409,009; U.S. Patent No. 5,259,837; U.S. Patent No. 4,955,385; U.S. Patent No. 4,706,681; U.S. Patent No. 4,582,061; U.S. Patent No. 4,407,294; U.S. Patent No. 4,401,124.

The bioptome and the optical probe can be disposed side-by-side or, preferably, concentrically such that the optical probe is located within the bioptome and can be extended between the jaws of the bioptome. Preferably, the optical bioptome is prepared so that when the jaws of the bioptome are opened the optical probe is extended past the open jaws to the target tissue, where the optical probe can then make a measurement, and when the jaws are closed the optical probe is retracted into its lumen within the body of the catheter or endoscope. When the optical probe and the jaws are side-by-side, however, the jaws need not open simultaneously with the extension of the optical probe, and need not close simultaneously with retraction of the optical probe. Thus, the bioptome and the optical probe can be disposed equally extended with regard to the distal tip of the catheter or endoscope, one can be disposed more extended than the other, or one or both can be extendible and retractable according to the needs of the user.

The optical probe and the bioptome can be modular or they can be integrated in a single assembly. As with the catheters, endoscopes and other devices described herein, each of the optical probe and the bioptome can be sterilized or destroyed after use.

When the optical bioptome is used for purposes such as fluorescence spectroscopy or Raman spectroscopy, the present invention provides, in one embodiment, a catheter or endoscope system comprising a light source that supplies

light at a proximal end of the catheter or endoscope, at least one illumination light guide, at least one collection light guide and the bioptome. Briefly, the illumination light guide transmits light from the proximal end of the catheter to the distal end, where the light is launched onto the target tissue. The collection light guide collects light that
5 emanates from the target tissue (such as reflected or fluorescent light) and transmits it to the proximal end of the catheter, where the light is made available for analysis. The illumination light guide and the collection light guide can be a single light guide, which means that the same light guide can function as both the illumination light guide and the collection light guide. Alternatively, the illumination light guide and the collection
10 light guide can be separate light guides.

In another embodiment, the present invention provides catheter systems comprising optical bioptomes that are capable of determining the orientation of the optical probe of the optical bioptome relative to the target tissue. The catheter systems comprise a light source that supplies light at a proximal end of a catheter, at least one
15 illumination light guide suitable for conducting light from the proximal end to a distal end of the catheter and for emitting the light from a distal end of the at least one illumination light guide, and at least three collection light guides, each collection light guide suitable for collecting light entering the distal end of the collection light guide and conducting the light to the proximal end of the catheter, wherein the collection light
20 guides are equally radially disposed around the at least one illumination light guide. As with many other aspects of this invention, the light guide ends are preferably flat cut and polished flush with the distal tip of the catheter.

In a functionally related embodiment, the present invention provides a catheter system suitable for emitting and collecting light, the catheter system
25 comprising a light source that supplies light at a proximal end of a catheter, at least three pairs of light guides, each pair comprising an illumination light guide suitable for conducting light from the proximal end to a distal end of the catheter and for emitting the light from a distal end of the illumination light guide and a collection light guide suitable for collecting light entering the distal end of the collection light guide and
30 conducting the light to the proximal end of the catheter, and wherein the distance from

the collection light guide to the illumination light guide is equal in the at least three pairs.

These embodiments of the invention are functionally related because they can be used to determine if the distal end is perpendicular to the target tissue and/or in contact with or near to the target tissue. The spacing between the light guides and the diameter of the light guides, which can be routinely selected by a person of ordinary skill in the art in light of the present disclosure, determine the depth layer of the target tissue from which optical property information is collected. As discussed above, independent measurement of the signal intensity from each collection light guide permits elucidation of the orientation of the distal tip and the target tissue, which can be used to indicate the quality of the measurement. Thus, in sum, these embodiments are preferred when the user desires to determine the orientation of the distal end (and the optical probe carried therein) relative to the target tissue and/or to selectively collect light from a certain desired depth of the target tissue.

Turning to some specific aspects of the invention, in one aspect the present invention provides a catheter or endoscope comprising a bioptome comprising opposed jaws and an extensible and retractable optical probe that extends distally to be disposed between the jaws when the jaws are open. The bioptome can comprise two or more opposed jaws, at least one of which is mobile, and the optical probe can extend and retract axially along the catheter in both distal and proximal directions. The jaws are opened when the optical probe is extended and the jaws are closed when the optical probe is retracted.

In another aspect, the present invention provides a catheter or endoscope comprising a bioptome comprising opposed jaws maintained in a closed position, one or more of the jaws comprising a central body and a distal scoop and an internal proximal surface that extends into the path of a push rod comprising the optical probe. The catheter or endoscope further comprises the push rod, which extends distally and retracts proximally along a path disposed between the jaws. The central body of one or more of the jaws comprises a projection, such as a thickened portion, that projects into the path of the push rod such that the push rod contacts the thickened portion as the

push rod extends distally, thereby forcing the jaws apart. When the push rod is retracted proximally, it separates from the thickened portion thereby allowing the jaws to close, and its near, or proximal, shoulder or surface contacts the internal proximal surface of the jaw, thereby causing the jaw to rotate about its hinge and close the jaws.

- 5 Preferably, the thickened portion of the jaw tapers in thickness in a proximal direction, such that the thickness of the thickened portion is greater at a distal end of the thickened portion than at a proximal end of the thickened portion, and the push rod tapers in thickness in a distal direction at an impact surface of the push rod that contacts the thickened portion of the central body of the jaw, such that the thickness of the push rod
10 is lesser at a distal end of the impact surface than at a proximal end of the impact surface.

- In a preferred embodiment, the proximal shoulder or surface of the push rod is inclined or angled in a proximal or backwards direction, and the internal proximal surface of the jaw has a corresponding proximal or backward incline. When the push
15 rod is retracted its proximal shoulder contacts and hooks or catches the internal proximate surface of the jaw, such that the proximal shoulder forms an overhang over the distal lip of the internal proximal surface of the jaw. Preferably the internal proximal surface of the jaw and the proximal shoulder of the push body incline at approximately the same angle to mate with each other upon the retraction. This
20 enhances the force transmitted from the push rod to the jaw that closes the jaw, and it enhances the contact between the push rod and the jaw such that there is a lower possibility of slippage. The angle or incline of the proximal shoulder can be implemented, for example, by providing one or more "swept back" wings or by providing a mushroom-like or girdle-like annulus. Preferably, the push rod comprises
25 an optical probe.

In another aspect of the invention, a liquid-carrying lumen that allows a bolus of non-fluorescing, non-reflecting liquid saline solution to be pumped to the distal tip of the catheter is co-luminal with the light guides. The structure of the catheter tip directs the liquid around the optical fibers and out to the tissue so that the resultant jet of

liquid pushes aside blood or other interfering material and acts as a liquid light path for transmission of light to, and collection of light from, the target tissue.

In a further aspect of the invention, the distal tip of the optical probe is covered with and bonded to an elastomeric balloon comprising an optically transmissive window that is preferably non-fluorescing and non-reflective. Upon opening of the jaws and extension of the light probe, a bolus of gas or liquid is pumped into the balloon to cause it to distend and thereby contact the window with the tissue. The liquid or gas, which can be air, in the balloon acts as an optically clear path to the tissue, while the balloon pushes blood and other interfering material out of the field of view.

10 This aspect of the invention can also be practiced with an optical probe that does not extend, provided that the balloon provides an optically clear pathway from the distal end of the optical probe to the target tissue, which typically requires the balloon to extend to or beyond the distal surface of the jaws of the bioptome.

The present invention also provides methods comprising the following steps. An optical probe is placed adjacent to, which herein means near, in contact with, or even removably attached to, a target tissue *in vivo*, via the manipulations of a handle, knob or other control mechanism located at the proximal end of a catheter or endoscope. Light is emitted from the distal end of the catheter or endoscope, which causes light to emanate from the target tissue, to provide emanating light. The emanating light is collected and then evaluated to determine whether the target tissue comprises the one or more characteristics indicating that the target tissue should be biopsied.

15 20

If the target tissue comprises one or more characteristics indicating that the tissue may be unhealthy (*i.e.*, in need of biopsy), additional methods further comprise obtaining the biopsy from the target tissue without removing the catheter from the body of the patient, and preferably without moving the distal end of the catheter within the patient. Keeping the distal end stationary between the optical scan and the biopsy facilitates obtaining the biopsy from the area of the target tissue that was illuminated by the optical scan, or the illumination area. Thus, these methods permit the same piece of tissue to be both scanned *in vivo* and biopsied.

25

In further aspects, preferably using apparatus described herein, the present invention provides methods of determining the orientation of an optical probe relative to a target tissue. The orientation of the optical probe means the angle and/or distance of the optical probe in comparison to the target tissue. The methods comprise the following steps. The jaws of the bioptome are placed adjacent to a target tissue. The jaws are opened and the optical probe is extended. Light is emitted, or launched, from at least one centrally disposed light emitter to the target tissue under conditions suitable to cause light (which can be, for example, reflectance light or fluorescent light) to emanate from the target tissue. Such emanating light is collected as it enters at least three (preferably six) radially disposed light collectors. Collected light is then analyzed to measure the relative intensity of the emanating light collected by each of the light collectors, which means the intensity of the emanating light is measured for each of the collection light guides and then assigned a value relative to the other light guides. Equal measurements for each of the collection light guides indicates that the optical probe is perpendicular to the target tissue; variance from equal gives the relative position of the probe. In view of the present disclosures, an artisan of ordinary skill can also vary the radial distance or diameter of one or more of the light collectors from the light emitter(s) and then account for such variation when determining the orientation of the optical probe, and still be within the scope of this discussion. In addition, the overall strength of the emanating light provides information about the distance of the optical probe from the target tissue, and therefore the measurement of the relative intensity of the collected emanating light can also provide a value of the absolute intensity of such light and the distance from optical probe to the target tissue.

In other methods capable of determining the orientation of an optical probe relative to a target tissue, the optical probe comprises at least three pairs of light emitters and light collectors. The light emitter in each of the at least three pairs is equally distanced from the light collector, which means that for each of the pairs, the light available for collection by the light collector is of the same relative intensity when the optical probe is perpendicular to the surface of the target tissue. Generally, the methods are performed as with the previous methods, except that illumination light

(typically equal in intensity, wavelength, etc., so that the emanating light induced by the illumination will be equal when the probe is perpendicular to the target tissue) is emitted from each of the at least three light emitters to the target tissue under conditions suitable to cause light to emanate from the target tissue, to provide emanating light.

- 5 The emanating light entering the at least three light collectors is collected. And, the relative intensity of the emanating light collected by each of the at least three light collectors is measured, therefrom providing for the determination of the orientation of the optical probe with respect to the target tissue.

The orientation of the optical probe to the target tissue is adequate to
10 provide sufficient data about the target tissue when the optical probe is close enough and perpendicular enough to the tissue that the emanating light does not contain artifacts that interfere with the interpretation of the emanating light. The optical probe has a suitable angle relative to the target tissue when the illumination light emitted by the probe strikes the target tissue generally evenly across the area of illumination such
15 that the strength of the induced return light from the target tissue is representative of the state of the tissue across the area of illumination and collection. Preferably, the illumination light emitted from the optical probe is emitted perpendicular to the target tissue.

In the event that the target tissue is found to comprise characteristics
20 indicating that a biopsy would be appropriate, then these methods optionally further comprise obtaining the biopsy, preferably of the same site that was optically scanned.

In this and other methods described herein, the methods are typically preferably performed on living animals, especially human patients. Thus, the illumination light is transmitted and the fluorescence, or other return light, is collected
25 *in vivo*.

In an embodiment that is preferred where the target tissue is a moving organ such as the heart, the timing of the optical scanning is controlled and synchronized with movement of the organism and/or the target organ to enhance the utility of the information that is collected and processed. Briefly, as discussed above,
30 measurements of target tissue are preferably made when the target tissue receives strong

illumination and then emits strong fluorescence (preferably a signal to noise ratio that is greater than about 5:1, further preferably greater than about 10:1) at a suitable orientation to be optimally collected and evaluated.

Thus, in a preferred embodiment, the illumination and collection are
5 both performed during a single diastole of a single heart beat (or other selected motion of the target tissue). This embodiment is particularly preferred when the target tissue is the heart. Determination of the diastole of the heart beat can be effected by a variety means that will be apparent to one of ordinary skill in the art in view of the present specification. For example, the user can detect an electrocardiogram of the heart beat of
10 the host, and then use one or more signals, such as the QRS wave or other identifiable event, of the electrocardiogram to initiate or trigger the steps of transmitting and collecting during a single diastole of the heart beat. Alternatively, the user can detect a pulse of the host using a blood pressure monitor, and then use the pulse to trigger the steps of transmitting and collecting. In a preferred embodiment, a pulse oximeter,
15 which measures the oxygen content of the blood, is used to provide the trigger that induces the scanning or data gathering.

In another aspect of the invention, another type of detection system, such as a non-optical imaging system, can be used. Depending upon the particular application, the detection system generally has a source for emitting a source energy at
20 the target tissue and a collector to receive a return energy from the target tissue. As set forth above, the energy source can be a fiber optic cable coupled to a light source and the collector can be a fiber optic cable coupled to a device for analyzing the collected light. The energy source can alternatively be an ultrasound emitter or a light at the distal end of the insertion element, and the collector can be an acoustic receiver or a
25 photo-cell. As such, the probes of the invention can be virtually any type of detecting or imaging systems.

Turning to the figures, Figures 1-28 depict various embodiments of catheters and endoscopes according to the present invention. For example, Figures 27 and 28 depict a general catheter or endoscope having a bioptome at its distal end and an
30 elongated catheter body 46, which contains an axially displaceable inner member

extending therethrough; in Figure 27 the bioptome and the optical probe are disposed side-by-side. The proximal end of the catheter body 46 and the inner member (which can be the light guide sleeve 50 depicted in Figures 1 and 11) are coupled to the scissors handle actuator 78 (multiple actuators can be used if desired). The proximal end of the
5 catheter or endoscope then proceeds to be connected to a light source 82 and an analysis station 84, which analyzes the light gathered by the optical probe disposed at the distal end of catheter 2.

Figures 1 to 5 depict one embodiment of an optical bioptome according to the present invention wherein the bioptome comprises jaws that are urged or spring-
10 loaded outwardly or apart. Figure 1 depicts the distal end of a catheter or endoscope having a catheter body 46 and a bioptome 4 disposed at the distal end thereof. The bioptome 4 has opposed jaws 8a and 8b, and encompasses optical probe 6, which probe is disposed between opposed jaws 8a and 8b. Optical probe 6 includes both an illumination light guide 10 and six collection light guides 12. The collection light
15 guides 12 are disposed radially about the illumination light guide 10, thereby providing a format in which the orientation of the optical probe can be determined relative to target tissue. The optical probe 6 includes a protective sheath 44 having a pair of grooves 36 therein that are sized to receive arms 38 that connect jaws 8a and 8b to jaw bases 48 (Figure 5). Protective sheath 44 is shorter than arms 38 so that retraction of
20 optical probe 6 from jaws 8a, 8b can be assured, and protective sheath 44 can be permanently attached to light guide sleeve 50, but preferably it is threadably, removably attached to light guide sleeve 50, which sleeve is preferably made of stainless steel. The jaws 8a and 8b comprise scoops 22 and cutting edges 62. When a plurality of light guides are disposed within the optical probe 6, they may be referred to as a light guide
25 bundle 42.

Turning to Figure 3, the optical bioptome depicted in Figures 1 and 2 is shown in closed position, which position is preferred when moving the bioptome within the body. Briefly, the arms 38 have been withdrawn into collar 40 thereby causing jaws 8a and 8b to close. The halves of collar 40 can be held together by an encircling band,
30 or can be bonded together. This protects the patient from the cutting edges 62. Collar

40 is attached to catheter body 46, and can either be permanently attached or removably attached, such as by threads, so that the collar can be detached and discarded after use. Also preferably, the threads of collar 40 (and the corresponding threads of catheter body 46, if any) are located in concert with the threads of protective sleeve 44 (and the corresponding threads of light guide sleeve 50, if any) such that the threads of each of
5 the collar and the protective sleeve are threaded simultaneously.

Figure 4 depicts a side view of the optical bioptome, wherein the distal tip of optical probe 6 can be seen projecting just slightly beyond the distal end of opposed jaw 8a of bioptome 4.

10 Figure 5 depicts an exploded view of the optical bioptome described above and shows the relation of many of the parts, including jaw base 48 and jaw base retainer 52, which holds jaw base 48 in a desired location along light guide sleeve 50, which sleeve is disposed within internal sleeve 66. Protective sleeve 44 has a proximal shoulder 64 that contacts jaw bases 48, such proximal shoulder 64 placing a proximally
15 directed pressure on jaw bases 48 (and therefore jaws 8a, 8b), such that jaws 8a and 8b are together when retracted proximally into collar 40 when optical probe 6 is retracted proximally into catheter 2. The proximal shoulder 64 accordingly defines a proximally facing engaging surface on the probe and the distal faces of the jaw bases 48 each define a distally facing contact surface of the jaw assembly. Likewise, distal end 74 of
20 protective sleeve 44 contacts and pushes the rear (proximal) edges of jaws 8a, 8b when optical probe 6 is extended distally by a user's actions at the proximal end of the catheter. Thus, the distal end 74 defines a distally facing engaging surface on the probe and the proximal edges of the jaws 8a and 8b each define a proximally facing contact surface of the jaw assembly.

25 Thus, beginning from the closed position of the catheter depicted in Figure 3, a user extends optical probe 6 distally, which causes distal end 74 of protective sleeve 44 to contact and push jaws 8 distally, which in turn extends jaws 8a, 8b beyond collar 40 which allows jaws 8a, 8b to open, as depicted in Figure 1. Because jaw bases 48 and jaw base retainer 52 are slidably secured to light guide sleeve 50,
30 when jaw bases 48 contact the internal edge of collar 40, the distal movement of jaws

8a, 8b is terminated and optical probe 6 continues to extend until it is about equidistant, or even slightly beyond (as in Figure 4), jaws 8a, 8b. Such distal movement of optical probe 6 is terminated when the distal edge of internal sleeve 66 contacts the proximal edge of jaw base retainer 52. Optical scanning, and obtaining of a biopsy, if indicated, then takes place. Optical probe 6 is then retracted such that the proximal shoulder 64 of protective sleeve 44 contacts jaw bases 48 and places a proximally directed pressure on jaw bases 48 (and therefore jaws 8a, 8b), thereby causing jaws 8a and 8b to be retracted proximally into collar 40 and forced together into a closed position.

Figures 25 and 26 depict an alternative optical bioptome similar to the embodiment depicted in Figures 1-5, except that the jaws are urged, or spring-loaded, inwardly or together. The movement of the optical probe and the bioptome relative to the catheter body 46 is effected in the same manner as in the embodiment in Figures 1-5, but the jaws 8a, 8b do not move apart until the tip of protective sleeve 44 contacts the rear, rounded shoulder 76 of jaws 8a, 8b which, as assisted by the rounded nature of the shoulder, permits protective sleeve 44 to force jaws 8a and 8b apart. Upon determining that a biopsy is needed, or merely to close the jaws 8a and 8b or to retract the catheter or endoscope from the patient, the jaws are weakly urged together by the spring-loading of arms 38, and then are forced together tightly by the retraction of arms 38 into collar 40. In addition, Figure 26 depicts one preferred embodiment for attaching collar 40 to catheter body 46, wherein a metal tip 86 is threaded onto catheter body 46, and then collar 40 is threaded into metal tip 86.

Figures 6-12 depict a second embodiment of the catheter or endoscope according to the present invention. The catheter of such figures includes opposed jaws 8a and 8b, an optical probe 6 and a bioptome 4. As depicted in Figures 7, 8 and 11, jaws 8a and 8b of bioptome 4 are forced apart when push rod 16 (which preferably, but not necessarily, comprises an optical probe 6) is extended distally within bioptome 4 such that push rod 16 contacts a projection, or thickened portion 18 of one or both of jaws 8a and 8b. For example, push rod 16 travels along a path 20 that is located within one or both of opposed jaws 8a and 8b. Opposed jaw 8a (and opposed jaw 8b, if desired) has a central body 14, and a scoop 22 located toward the distal end of the jaw.

Within the central body 14 of jaw 8a, there is a thickened portion 18 that projects into path 20 of optical probe 6 and push rod 16. Accordingly, when push rod 16 contacts thickened portion 18, push rod 16 forces jaws 8a and 8b apart in a cam-like action. Push rod 16 can be advanced distally and retracted proximally within the catheter 2 via the use of a scissors handle actuator 78 as in Figures 27 and 28, or by use of knobs, handles, buttons and other mechanisms known in the art, which can also be used for the embodiments shown in the other figures and otherwise disclosed herein. In order to close jaws 8a and 8b, push rod 16 is retracted in a proximal direction. This removes push rod 16 (including optical probe 6 if present) from jaws 8a, 8b, and also causes proximal shoulder 72 of push rod 16 to contact flat shoulder 70 of jaws 8a, 8b. Upon such contact, push rod 16 exerts a cam-like force on proximal shoulder 72 that causes jaws 8a, 8b to rotate about pins 54 and hinges 56 and thereby close jaws 8a, 8b. Such force also maintains jaws 8a, 8b closed during insertion and removal of the catheter.

In one embodiment, and as depicted in Figures 7, 8 and 11, thickened portion 18 preferably tapers from its proximal end 28 to its distal end 26, thereby providing a taper 24 such that the cam-like action force on jaws 8a and 8b by push rod 16 is accomplished gradually. Such an arrangement also minimizes the likelihood that push rod 16 will "catch" on thickened portion 18. Alternatively, or in combination with taper 24, push rod 16 also has a taper from a distal end 32 to a proximal end 34 of the impact surface 30 of push rod 16, which is the surface that contacts thickened portion 18 of jaws 8a (and 8b if desired). Preferably, as depicted in Figure 7, 8 and 11, the optical bioptome of the invention includes a taper in both the thickened portion jaws of 8a and 8b and in the impact surface 30 of push rod 16.

Opposed jaws 8a and 8b can be attached to a hinge base 60 via pins 54 inserted through hinge pin passages 55, thereby creating a hinge 56, although other mechanisms for attachment of the jaws to the bioptome will be readily apparent to persons of ordinary skill in view of the present specification. Preferably, the proximal end of jaws 8a, 8b is sized such that it abuts the distal surface of hinge base 60, thereby inhibiting the outward motion of jaws 8a, 8b and preventing them from opening too widely. In addition, hinge base 60 can be inserted into connector 58, which connector

attaches hinge base 60 to catheter 2. Such connection can be permanent, but preferably the connection is non-permanent, for example via the use of threads. This enhances use of the optical bioptome in a modular manner, in that the bioptome is easily removable and can be discarded after use, while the optical probe (and the remainder of the catheter) can be cleaned and sterilized for future use.

Figures 9 and 10 depict first and second side views of the catheter depicted in Figures 6-12, showing the arrangement of the hinges and jaws, while Figure 11 depicts an exploded isometric view of the catheter depicted in Figures 6-12.

Figures 13-19 depict another embodiment of the catheter or endoscope according to the present invention. As with the catheter or endoscope depicted in Figures 6-12, the catheter or endoscope of Figures 13-19 includes opposed jaws 8a and 8b, a push rod 16 and a bioptome 4. The jaws 8a and 8b of bioptome 4 are forced apart when push rod 16 (which preferably, but not necessarily, comprises an optical probe 6) is extended distally along displacement path D-D within pathway 20 such that the impact surface of distal edge 106 (Figures 17-19) of wing 102 contacts distal incline 96 (Figures 15 and 16) of thickened portion 18 of jaws 8a and 8b, thereby forcing the jaws apart. When push rod 16 is retracted within path 20, proximal edge 104 (Figures 18 and 19) of wing 102 (which edge constitutes a proximal shoulder of push rod 16) contacts and catches a corresponding proximal incline 94 (which is an internal proximal surface of central body 14 shown in Figure 15), thereby providing an enhanced pressure that forces jaws 8a and 8b towards one another. Due to such "catching" action, the proximal edge 104 of wing 102 forms an overhang over the distal lip 122 (Figure 15) of proximal incline 94.

Preferably, the proximal edge 104 projects radially outward from the push rod body and is inclined toward the proximal end of the catheter at an acute angle 112 with respect to a displacement axis D-D (Figure 18) of the push rod 16. Similarly, the proximal incline 94 extends radially outward from its distal lip 122 and toward the proximal end of the catheter at a corresponding acute angle 114 with respect to the displacement axis D-D of the push rod 16. Also preferably, acute angles 112 and 114 are the same. The leading edge 106 of the wing 102 preferably projects radially

outwardly from the body of push rod 16 and is inclined toward the proximal end of the catheter or endoscope at an acute angle 116 with respect to the displacement axis D-D. The distal incline 96 of the thickened portion 18 can also be inclined toward the proximal end at an acute angle 118 with respect to the displacement axis D-D.

5 Preferably, acute angles 116 and 118 are also the same.

When jaws 8a and 8b are closed, an opening 92 in each jaw 8a and 8b receives a wing 102 of the push rod 16, and the pathway 20 in each jaw 8a and 8b receives a portion of the push rod body 107. In the embodiment depicted in Figures 13-16, opening 92 completely transects central body 14 of jaws 8a and 8b, but it is not
10 necessary that it do so. Jaws 8a and 8b are attached to hinge base 60 via a hinge pin 54 (Figure 14) that is inserted through hinge base 60 and hinge pin passage 55 in tongue 90 of jaws 8a, 8b. In alternative embodiments, wing 102 can circumscribe the body of push rod 16, to give a mushroom like appearance to the push rod.

Figure 20 depicts yet another embodiment of a catheter or endoscope
15 according to the present invention, wherein the opposed jaws of the bioptome comprise only a single mobile jaw. In particular, in Figure 20, only jaw 8a moves relative to jaw base 60. In the embodiment shown in Figure 20, scoop 22 of jaw 8a has a tooth 108 that corresponds to a receiving surface 110 of jaw base 60, such that the opening and closing of the jaw permits push rod 16 (and optical probe 6 when carried therein) to
20 travel in a straight line as it traverses scoop 22. In alternative embodiments, however, the path of the push rod 16 need not be straight if so desired. In still other embodiments, the bioptome can contain three or more opposed jaws. In the embodiment in the figure, jaw base 60 tapers at its proximal end 100, where it abuts a connector or other desired surface of the catheter or endoscope.

25 Figure 22 depicts one preferred embodiment for attaching a bioptome as described herein to a catheter body 46. Briefly, hinge base 60 is threaded such that it can be screwed into a catheter tip 80, which catheter tip, in turn, is threaded, bonded or otherwise attached to catheter body 46. Similarly, Figures 22, 23 and 24 depict another preferred embodiment for attachment of components of the optical bioptome to the
30 catheter body. Briefly, hinge base 60 is threaded to be screwed directly onto catheter

body 46, while push rod 16 and light guide sleeve 50 are respectively threaded so that push rod 16 can be threaded onto light guide sleeve 50. In one preferred embodiment, push rod 16 is preferably square-shaped and sized to fit snugly in path 20, or otherwise shaped to non-rotatably slide in path 20 as in Figures 13-20, such that push rod 16 is
5 rotated simultaneously with rotation of the bioptome assembly while screwing such onto the light guide sleeve 50 and catheter body 46, respectively. The methods of attachment depicted in Figures 21-24 enhance the use of the optical bioptome in a modular manner, as discussed above.

Turning to a general discussion related to some preferred scanning
10 methods and to some preferred subsidiary apparatus, healthy tissue exhibits a characteristic fluorescence response in reply to excitation with ultraviolet to visible light. However the fluorescence response and/or the Raman spectroscopic response of diseased, injured or otherwise harmed tissue changes relative to the healthy tissue. Thus in one preferred embodiment, the optical probe of the present invention is directed
15 to the measurement and analysis of such response. Typically, a light guide for such embodiments can be an optical fiber, fiber bundle, liquid light guide or hollow reflective light guide or lens system, or other pathways suitable for carrying information related to light generated scans and images. Additionally, as noted above, the optical probes of the present invention can also be used for any other optical scanning or image
20 gathering. Therefore, the optical probe can comprise a lens or other image sensor, and the term "light guide" includes electronic leads that electronically carry an image such as for a video camera or other video display.

Transmitting the light to the target tissue comprises delivering light from a light source (such as a lamp) to the tissue. The lamp can be carried by the catheter or
25 endoscope and shown onto the target and tissue; or, preferably, the lamp is located at the proximal end of the catheter or endoscope and transmitted via one or more illumination light guides to the target tissue.

The light that is transmitted to the target tissue typically comprises light from ultraviolet light through visible light and can induce fluorescence, reflectance or
30 other response in the target tissue. Preferably, the light does not comprise UV light

because such light can be harmful to the tissue. Conditions to induce fluorescence in tissue, when desired, are well known in the art. See, e.g., U.S. Patent No. 4,836,203; U.S. Patent No. 5,042,494; U.S. Patent No. 5,062,428; U.S. Patent No. 5,071,416; U.S. Patent No. 5,421,337; U.S. Patent No. 5,467,767; U.S. Patent No. 5,507,287.

5 In further embodiments, as discussed above, the devices of the present invention comprise the use of non-fluorescence detection systems. One example of such a system is Raman spectroscopy. Mahavedan-Jansen, A. and Richards-Kortum, R., *J. Biomed. Optics* 1(1):31-70, 1996. Briefly, Raman spectroscopy detects the vibrational signatures of particular molecules inside a selected tissue, thereby providing
10 chemical and other information about the tissue. Preferably, the methods are implemented using a CCD array as a detector and appropriate aspects of volume phase holographic spectrography. Typically, Raman spectroscopy is performed using near IR light. Other preferred detection systems include Optical Coherence Tomography (OCT) (Fercher, *J. Biomed. Optics* 1(2):157-173, (1996)), the determination of the lifetime
15 decay of the autofluorescence emitted by the target tissue, and the induction of fluorescence using multiple photons that, when combined, deliver a desired energy to the fluorophore in the target tissue.

The target tissue is preferably from a human being, but the invention can be practiced for the benefit of other animals such as dogs, cats, horses and cows.

20 The methods, optical biotomes and other apparatus described herein can be operably linked to a computer containing at least one computer implemented program that implements at least one facet of the methods, optical biotomes and/or other apparatus. In a preferred embodiment, the program is able to determine the spectrum of light collected by the collection light guide, determine an intensity of light
25 collected by the collection light guide, compare the relative intensity of light collected by a plurality of collection light guides and/or time when light is to be transmitted along the light guides in concert with a pulse or electrocardiogram.

Generally speaking, a computer suitable for use with the various aspects of the present invention comprises a user interface, a system control, and devices for
30 data acquisition, processing and management. Briefly, the user interface typically

comprises devices such as probes, keyboards and screens for the entry and display of patient data and session information, system parameters and current control parameters and data collected. The system control typically effects system timing, light source pulsing and data acquisition timing. Data acquisition typically concerns
5 synchronization with physiological signals, signal conditioning and preprocessing, and data acquisition and storage. Data Processing typically concerns data quality verification, data signal processing and data analysis. Data management typically concerns a structured data storage, data integrity check, data security, data backup and data reporting.

10 The following discussion sets forth some of components that are advantageous for use with the methods and apparatus of the present invention. Briefly, systems suitable for implementation of optical scanning such as is described herein generally comprise a light source to generate appropriate excitation wavelength(s), a detector that selects and measures the appropriate wavelengths of the fluorescence
15 emitted, and, preferably, a data processing and control system with software that controls the timing of illumination and detection and processes the acquired data.

Light Sources

The present invention can use any light source that provides a light that illuminates a target tissue. In one preferred embodiment, the illumination light induces
20 fluorescence in the target tissue. For some aspects of the invention, the light source need not induce fluorescence, but may instead cause reflectance or other light to be emitted from the target tissue. Selection of an appropriate light source is well within the ordinary skill in the art in view of the present specification. With regard to light sources that induce fluorescence, the light source can be selected to provide light from
25 ultraviolet (UV) through visible light. Preferably, the light comprises blue or near-UV light. Also preferably, and particularly for *in vivo* aspects of the invention, the light does not comprise UV light because such light can induce cancer or other problems within the patient organism, which is preferably a human being. Further preferably, the light consists essentially of blue light and/or green light.

Some examples of preferred light sources to generate the required excitation energy include a pulsed xenon flashlamp equipped with wavelength selection filters, a CW (continuous wave) mercury or xenon arc lamp equipped with wavelength selection filters, a Blue or UV CW laser, and a Blue or UV pulsed laser. These are discussed below. The light source preferably has an indexed mechanical coupling adapter to ensure that the illumination light guide is positioned to maximize the light entering the fiber, and is preferably controlled by system software, which controls pulse timing of the arc lamp power supply.

A pulsed xenon flashlamp comprises a sealed housing arc lamp and power supply. The arc lamp typically has an arc length of less than 2 mm and is optionally equipped with an integral reflector to maximize energy directed toward the illumination light guide of the catheter or optical probe. An optical filter or series of filters placed in the optical path can select the wavelength of the illumination light. The energy emitted by the arc lamp is collected and focused by a lens system. In a preferred embodiment suitable for use with the present invention, the lenses are selected to direct the energy in a converging cone into an illumination light guide, with an apex angle that is less than or equal to the acceptance angle of the illumination light guide as defined by the numerical aperture of the illumination light guide.

A CW mercury or xenon arc lamp light source comprises a sealed housing arc lamp and power supply. The arc lamp typically has an arc length of less than 2 mm and is optionally equipped with an integral or external reflector to maximize energy directed toward the illumination waveguide of the catheter or optical probe. An optical filter or series of filters placed in the optical path can select the wavelength of the illumination light. The energy emitted by the arc lamp is collected and focused by a lens system. The lenses are selected to direct the energy into the illumination light guide in a converging cone with an apex angle that is less than or equal to the acceptance angle defined by the numerical aperture of the illumination light guide. In one embodiment, the lamp power supply operates continuously with no pulsing. Alternatively, the lamp can be powered by a sinusoidally varying current/voltage, which can also enhance the blue wavelength emission of the lamp.

A blue or UV CW laser light source comprises a laser that emits light in the blue or near ultraviolet wavelengths. Wavelength selection can be accomplished by using a laser such as a Helium-Cadmium (HeCd) laser or a Krypton-Argon laser that emits in the blue portion of the spectrum. Alternatively, a dye laser pumped by a shorter wavelength laser wherein wavelength selection is a function of dye characteristics and cavity monochrometer tuning can be used. The energy emitted by the laser is collected and focused by a lens system. The lenses are selected to direct the energy into the illumination light guide in a converging cone with an apex angle that is less than or equal to the acceptance angle defined by the numerical aperture of the illumination light guide. The laser can be equipped with a manual and/or computer controlled shutter.

A blue or UV pulsed laser light source comprises a laser that emits light in the blue or near ultraviolet wavelengths. The laser emits short duration pulses, preferably under software program control. Wavelength selection can be accomplished by using a dye laser pumped by a shorter wavelength laser wherein wavelength selection is a function of dye characteristics and cavity monochrometer tuning. Alternatively, a longer wavelength laser equipped with a frequency doubling system and/or an optical parametric oscillator (OPO) can be used. The energy emitted by the laser is collected and focused by a lens system. The lenses are selected to direct the energy into the illumination light guide in a converging cone with an apex angle that is less than or equal to the acceptance angle defined by the numerical aperture of the illumination light guide.

Detectors

Detectors suitable for use with the present invention separate the fluorescence light emitted by the target tissue, and typically conducted to the detector from the target tissue by a collection light guide, into wavelength regions of interest and produces a signal proportional to the fluorescence emission of each of the regions of interest. The present invention can use more than one detector if desired. The detector is typically controlled by the system software so that start of acquisition and integration

time can be synchronized with the shuttering and pulsing of the illumination system and with the physiological triggers. Exemplary detectors include a charge coupled device (CCD), charge injection device (CID), intensified CCD detector, photomultiplier tube (PMT) detector array, photo-diode array (PDA), intensified PDA and an avalanche
5 photo-diode (APD) array.

The fluorescence light collected by the collection light guide can be directed to a wavelength dispersive grating or prism and the resultant spectrally distributed light is projected onto the selected detector array(s), which has been calibrated for wavelength and intensity. The resulting signal then typically undergoes
10 signal processing and discriminant analysis by the system software to determine whether the signal comprises the optical characteristics of tissue undergoing rejection.

In a preferred embodiment, the fluorescence is collected by multiple collection light guides and is projected onto the selected detector array such that the signal for each collection light guide can be analyzed independently. This type of
15 multiple collection light guide/ 2-D detector array (which can also be implemented with other types of detector arrays) can be particularly helpful for analysis of information to elucidate probe orientation, distance and mobility relative to the target tissue.

In another preferred embodiment, the fluorescence light from the target tissue is directed into an optical beam splitter that divides the light into two or more
20 spectral regions of interest. The spectrally separated components are then each directed to discrete detectors. In preferred embodiments, detectors can be silicon detectors, photomultiplier tubes or avalanche photo diodes, although other detectors can also be used advantageously with this embodiment of the invention.

System Controller Program

25 The system controller program controls the timing of the emission of the light that induces emanation of light from target tissue, typically by controlling the pulsing or shuttering of the light source. It can also control and synchronize the timing of emanation light acquisition and detector integration with the operation of the light source, and in a preferred embodiment control and synchronize the timing of such

actions with external or internal physiological measurement triggers, such as an electrocardiogram (ECG) or the pulse generated by the heart beat. In one preferred embodiment, the measurement of the pulse comprises the use of a pulse oximeter. In the ECG triggering mode, the software synchronizes illumination and collection windows with specific signals, or waves, within the ECG, such as the QRS wave. One advantage of an ECG trigger is that the ECG can be obtained from an external patient electrocardiograph monitoring device or system. Pulse oximeter triggering mode permits the user to trigger timing of various actions from an external pulse oximeter monitoring device or system.

Using the system controller program, the user can set a time interval for desired events. For example, the user can set a time interval after the physiological trigger or after initiation of data acquisition when the light source will be pulsed or shuttered, when data acquisition will begin, and/or when data will be measured, integrated and/or analyzed. Alternatively, such interval(s) can be set automatically by the system controller program.

After data acquisition, in one embodiment, the system controller program can process the data to determine the relative responses of the intensity of the spectral regions of interest. This information can then be compared to the responses characteristic of normal and abnormal tissue and then shown by a display, such as a numerical or graphic display, to assist the surgeon in evaluating the tissue and/or determining appropriate sites for biopsy.

The following Example is offered by way of illustration, and not by way of limitation.

25

EXAMPLE

OPTICAL BIOPSY *IN VIVO* OF A HUMAN BEING

After determining that the patient is not excluded from the procedure, perform a standard diagnostic cardiac catheterization procedure in order to introduce an optical bioprobe into the heart. Such procedure can comprise a standard right heart

30

catheterization performed percutaneously from the right internal jugular vein as described below. A 9 F sheath is used initially, which can accommodate a standard 7 F end-hold catheter or 7 F balloon-directed floating thermodilution catheter.

A cap is placed over the patient's hair and a pillow is positioned under the shoulders and neck in order to slightly hyperextend the neck. Care is taken to position the head in line with the long axis of the body, with the patient facing to the left. The right side of the neck is prepped and draped using standard sterile technique. Gentle pressure is then placed on the patient's mandible, and the patient is asked to raise his head slightly off the pillow (no more than 2 in.). This causes the sternomastoid muscle to contract, thus making it easier to identify landmarks and to mark the position to introduce the sheath. A point on the lateral border of the median head of the sternomastoid muscle at least 6 cm above the clavicle is marked. The area is infiltrated with 2% xylocaine using a 25-gauge needle. A 22-gauge, 1 ½-in. needle is then attached to the syringe and xylocaine is infiltrated deeply. Care is taken not to enter the carotid artery. The needle is angled caudal and slightly lateral in an attempt to locate the right internal jugular vein, which lies directly under the lateral head of the sternocleidomastoid muscle.

After the area is adequately anesthetized a small stab wound is made in the skin with a #11 scalpel blade and the subcutaneous tissue is spread apart with a small straight clamp. A 10-cc syringe containing a small amount of saline is attached to a 22-gauge needle. The patient is instructed to perform the Valsalva maneuver, in order to increase venous pressure. It is also helpful to raise the patient's legs, thus further increasing venous pressure. The needle is then advanced slowly, angling the tip both caudal and slightly lateral so that it penetrates just under the lateral head of the sternomastoid muscle. Constant suction is maintained on the syringe in order to identify when the needle first enters the internal jugular vein. The needle is not advanced through the back wall of the vein, thus minimizing the possibility of bleeding into the carotid sheath.

The syringe is detached and the needle left in place in order to act as a guide. An 18-gauge Amplatz or Courmand needle is attached to the syringe. Using

constant suction, the needle is advanced slowly following the course of the 22-gauge needle. When the internal jugular vein is entered, a short straight guide wire is passed through the 18-gauge needle, the needle removed, and the false catheter-dilator and sheath are then positioned in the internal jugular vein using standard technique. The
5 side-arm of the sheath is fitted with a stopcock to prevent an air embolus. The side-arm and sheath are then flushed with heparanized saline.

The optical bioptome is prepared by curving it at a 45° angle approximately 7 cm from the tip. The bend is in alignment with the optical bioptome handle, thus facilitating proper manipulation of the tip in the heart. The patient is asked
10 to suspend breathing and the optical bioptome is advanced quickly into the sheath, pointing the tip towards the lateral border of the heart (the patient's right side). Fluoroscopy can be used at this point in order to ensure that the optical bioptome does not inadvertently enter the right subclavian vein. When the optical bioptome is in the mid to lower third of the right atrium, the handle is rotated counterclockwise (anterior)
15 to point the tip medially. The tip of the optical bioptome is then advanced across the tricuspid valve. Occasional difficulty in crossing the tricuspid valve will be encountered. A slightly different bend on the optical bioptome or rotating the optical bioptome at a different level in the right atrium will facilitate crossing the tricuspid valve.

20 After crossing into the right ventricle the optical bioptome handle is rotated further counterclockwise so that it is now pointing posteriorly; the optical bioptome tip should also be pointed in this direction. The posterior position of the optical bioptome tip can be verified using a C-arm type fluoroscope is available. The tip is then advanced until it meets resistance (at this point the operator should feel the
25 cardiac impulse) or until ventricular premature depolarizations are induced. The tip is now in the area of the right ventricular apex pointing towards the ventricular septum. On fluoroscopy the tip should be at the level or slightly caudal to the top of the left diaphragm.

The distal surface of the jaws of the optical bioptome is then contacted
30 with the surface of the ventricular septum, and the optical probe is extended, thereby

forcing apart the jaws of the bioptome. The optical probe is then contacted with the surface of the ventricular septum (if not already in contact), and an optical biopsy is performed.

An optical scan of the tissue is then obtained. The resulting scan is
5 analyzed to determine if the tissue exhibits one or more problematic characteristics. In an alternative embodiment, the optical bioptome is attached to an endoscope and the optical biopsy comprises obtaining an image of the target area and reviewing the image for evidence of problems that indicate a biopsy should be obtained.

In the event that the optical biopsy suggests that tissue biopsy is
10 indicated, the optical probe is retracted and the jaws of the bioptome are closed, preferably without loss of contact between the bioptome and the ventricular wall. This tends to straighten the bend in the optical bioptome, pointing the tip more towards the apex of the right ventricle. Such straightening of the optical bioptome can also be effected prior to obtaining the biopsy, if desired. Occasionally, it is necessary to pause
15 approximately 2 to 5 sec to allow the jaws to close completely. The bioptome is then withdrawn rapidly and in the same motion rotated clockwise (anteriorly) back to the right atrium. Initially, significant resistance may be experienced, but then there will be a sudden release of tension and the bioptome can be quickly withdrawn from the right ventricle. The patient is then asked to suspend breathing and the bioptome is withdrawn
20 from the sheath. The jaws of the bioptome are opened and the size of the sample is examined. The sample is removed using fine forceps. Care is taken not to crush the sample. It is then placed in room temperature fixative for later study.

When manipulating the bioptome into the right ventricle, it is preferred that the bioptome is rotated anteriorly, thus avoiding accidental entry into the coronary
25 sinus. The biopsy will typically be taken from the ventricular septum in order to avoid the thin free wall of the right ventricle. It is also preferred to remove the biopsy from the apex of the right ventricle in order to avoid the conducting system.

If indicated from the optical biopsy, from three to five tissue biopsy specimens are obtained, each measuring approximately 1 to 2 mm³. Samples are
30 assayed for light and electron microscopy and one specimen frozen for possible

subsequent study. Specimens may also be obtained for viral culture or other specialized procedures.

At the conclusion of the procedure the thorax is fluoroscoped to look for evidence of either pericardial effusion, pleural effusion, or pneumothorax. If any
5 complication is suspected a standard chest film or echocardiogram may be obtained. The patient is then put in a sitting position to lower venous pressure, asked to suspend breathing, and the sheath is removed. Pressure is applied to the area above and below the puncture site for at least 10 min. The puncture site is then covered with a Band-Aid-type bandage.

10 Although the present invention had been described in some detail by way of illustration and example for purposes of clarity and understanding, it will be readily apparent to those of ordinary skill in the art in light of the teachings of this invention that certain changes and modifications may be made thereto without departing from the spirit or scope of the appended claims.

CLAIMS

What is claimed is:

1. A catheter comprising at a distal end of the catheter a bioptome comprising opposed jaws and an optical probe, wherein the bioptome and the optical probe are extensible and retractable relative to each other, and wherein the optical probe extends distally to be disposed between the jaws when the jaws are open, wherein the optical probe comprises at least one illumination light guide suitable for conducting light from a proximal end to a distal end of the catheter and for emitting the light from a distal end of the illumination light guide and at least one collection light guide suitable for collecting light entering a distal end of the collection light guide and conducting the light to the proximal end of the catheter, wherein the jaws are opened when the optical probe when the optical probe is extended and the jaws are closed by the optical probe when the optical probe is retracted.
2. The catheter of claim 1 wherein the illumination light guide and the collection light guide are a single optic fiber.
3. The catheter of claim 1 wherein the optical probe comprises at least three collection light guides, wherein the collection light guides are equally radially disposed around the at least one illumination light guide.
4. The catheter of claim 1 wherein the optical probe comprises at least three pairs of light guides, each pair comprising at least one of the illumination light guide and the collection light guide, and wherein the distance from the collection light guide to the illumination light guide is equal in each of the at least three pairs.
5. A catheter comprising a bioptome comprising opposed jaws that are maintained in a closed position, at least one of the jaws comprising a central body, a distal scoop and an internal proximal surface, the catheter further comprising a push rod that extends distally and retracts proximally along a path disposed between the jaws, wherein the

central body of the at least one jaw comprises a projection that projects into the path of the push rod such that the push rod contacts the projection as the push rod extends distally thereby forcing the jaws apart and wherein a proximal shoulder of the push rod contacts the internal proximal surface of the jaw as the push rod is retracted proximally relative to the jaw, thereby causing the jaws to close.

6. The catheter of claim 5 wherein at least two jaws each comprise a central body comprising a thickened portion defining the projection and the scoop.

7. The catheter of claim 6 wherein the thickened portion tapers in thickness in a proximal direction, such that the thickness of the thickened portion is greater at a distal end of the thickened portion than at a proximal end of the thickened portion.

8. The catheter of claim 5 wherein the push rod tapers in thickness in a distal direction at an impact surface of the push rod that contacts the projection of the central body of the jaw, such that the thickness of the push rod is lesser at a distal end of the impact surface than at a proximal end of the impact surface.

9. The catheter of claim 5 wherein the proximal shoulder of the push rod projects from the body of the push rod toward the proximal end at a first acute angle with respect to a displacement axis of the push rod, and wherein the internal proximal surface of the jaw is inclined toward the proximal end at a second acute angle with respect to the displacement axis, such that when the proximal shoulder and the internal proximal surface contact one another during proximal retraction of the push rod relative to the jaw, the proximal shoulder forms an overhang over at least a portion of the internal proximal surface of the jaw.

10. The catheter of claim 9 wherein the first acute angle and the second acute angle are about the same.

11. The catheter of claim 5 wherein the push rod is an optical probe that comprises at least one illumination light guide suitable for conducting light from a proximal end to a distal end of the catheter and for emitting the light from a distal end of the illumination light guide and at least one collection light guide suitable for collecting light entering a distal end of the collection light guide and conducting the light to the proximal end of the catheter.

12. The catheter of claim 5 wherein the illumination light guide and the collection light guide are a single optic fiber.

13. The catheter of claim 5 wherein the optical probe comprises the at least one illumination light guide and at least three collection light guides, wherein the collection light guides are equally radially disposed around the at least one illumination light guide.

14. The catheter of claim 5 wherein the optical probe comprises at least three pairs of light guides, each pair comprising at least one of the illumination light guide and at least one of the collection light guide, and wherein the distance from the collection light guide to the illumination light guide is equal in each of the at least three pairs.

15. An endoscope comprising a bioptome comprising opposed jaws and an extensible and retractable optical probe that extends distally to be disposed between the jaws when the jaws are open, wherein the optical probe comprises an image sensor and one or more light guides to transmit an image gathered by the image sensor from the distal end of the endoscope to the proximal end of the endoscope, wherein the jaws are opened when the optical probe is extended and the jaws are closed by the optical probe when the optical probe is retracted.

16. An endoscope comprising a bioptome comprising opposed jaws that are maintained in a closed position, at least one of the jaws comprising a central body, a distal scoop and an internal proximal surface, the endoscope further comprising a push rod

comprising an optical probe that extends distally and retracts proximally along a path disposed between the jaws, wherein the optical probe comprises an image sensor and one or more light guides to transmit an image gathered by the image sensor from the distal end of the endoscope to the proximal end of the endoscope, and wherein the central body of the at least one jaw comprises a thickened portion that projects into the path of the push rod such that the push rod contacts the thickened portion as the push rod extends distally thereby forcing the jaws apart and wherein a proximal shoulder of the push rod contacts the internal proximal surface of the jaw as the push rod is retracted proximally relative to the jaw, thereby causing the jaws to close.

17. The endoscope of claim 16 wherein at least two jaws each comprise a central body comprising the thickened portion and the scoop.

18. The endoscope of claim 16 wherein the thickened portion tapers in thickness in a proximal direction, such that the thickness of the thickened portion is greater at a distal end of the thickened portion than at a proximal end of the thickened portion.

19. The endoscope of claim 16 wherein the push rod tapers in thickness in a distal direction at an impact surface of the push rod that contacts the thickened portion of the central body of the jaw, such that the thickness of the push rod is lesser at a distal end of the impact surface than at a proximal end of the impact surface.

20. The endoscope of claim 15 wherein the proximal shoulder of the push rod projects from the body of the push rod toward the proximal end at a first acute angle with respect to a displacement axis of the push rod, and wherein the internal proximal surface of the jaw is inclined toward the proximal end at a second acute angle with respect to the displacement axis, wherein the first acute angle and the second acute angle are about the same such that, when the proximal shoulder and the internal proximal surface contact one another during proximal retraction of the push rod relative to the jaw, the proximal shoulder forms an overhang over at least a portion of the internal proximal surface of the jaw.

21. The endoscope of claim 20 wherein the first acute angle and the second acute angle are about the same.

22. An insertion device for analyzing and selectively taking a biopsy of a target tissue internally within a patient, comprising:

a bioptome having a base configured to be coupled to a distal end of an insertion element and a jaw assembly attached to the base, the jaw assembly having a moveable first jaw and a second jaw opposed to the first jaw, the first jaw having a cup with a cutting edge; and

an detection system having an energy source for emitting a source energy and a collector for receiving a return energy, the detection system being coupled to and positioned at least in part within the jaw assembly, and at least one of the detection system and the jaw assembly being moveable with respect to the other along a displacement path between a first position and a second position, the first jaw being biased apart from the second jaw in an open arrangement in the first position to expose the energy source and the collector to the target tissue, and the first jaw being biased against the second jaw in a closed arrangement in the second position to enclose the energy source and the collector within the jaw assembly, wherein the cup of the first jaw selectively removes a portion of the target tissue to biopsy the patient.

23. The insertion device of claim 22 wherein the detection system comprises an optical probe in which the energy source and the collector comprise a single fiber optic fiber.

24. The insertion device of claim 22 wherein the second jaw of the jaw assembly is fixed.

25. The insertion device of claim 22 wherein the second jaw of the jaw assembly is a moveable with respect to the base and includes a cup with a cutting edge, the first and second jaws moving between open and closed arrangements.

26. An insertion device for analyzing and selectively taking a biopsy of a target tissue internally within a patient, comprising:

a bioptome having a base configured to be coupled to a distal end of an elongated insertion element and a jaw assembly attached to the base, the jaw assembly having a moveable first jaw and a second jaw opposed to the first jaw, the first jaw having a cup with a cutting edge, a proximally facing contact surface and a distally facing contact surface; and

an detection system coupled to the bioptome and positioned at least in part within the jaw assembly, the detection system including an energy source for emitting a source energy, a collector for receiving a return energy, a distally facing engaging surface configured to engage the proximally facing contact surface and a proximally facing engaging surface configured to engage the distally facing contact surface, at least one of the bioptome and the detection system being moveable with respect to the other along a displacement path, the distally facing engaging surface engaging the proximally facing contact surface as relative motion occurs in a first direction to drive the first jaw into an open position exposing the energy source and the collector, and the proximally facing engaging surface engaging the distally facing contact surface as relative motion occurs in a second direction to drive the first jaw against the second jaw in a closed position, the energy source and the collector being housed the jaw assembly in the closed position and the cup of the first jaw being capable of removing a portion of the target tissue from the patient as the first jaw closes against the second jaw.

27. The insertion device of claim 26 wherein the detection system comprises an optical probe in which the energy source and the collector comprise a single fiber optic fiber.

28. The insertion device of claim 26 wherein the second jaw of the jaw assembly is fixed.

29. The insertion device of claim 26 wherein the second jaw of the jaw assembly is a moveable with respect to the base and includes a second proximally facing

contact surface, a second distally facing contact surface, and a cup with a cutting edge, and wherein the detection system engages the second jaw to move the second jaw between open and closed positions corresponding to the open and closed positions of the first jaw.

30. A method for determining whether a target tissue exhibits one or more characteristics indicating that the target tissue be biopsied, the method comprising:

- a.) placing the opposed jaws of the catheter of any one of claims 1, 5, 9 or 11 or the endoscope of any one of claims 15, 16 or 20 adjacent to a target tissue *in vivo*;
- b.) extending the optical probe and opening the jaws of the catheter or endoscope;
- c.) emitting light from the distal end of the catheter or endoscope under conditions suitable to cause light to emanate from the target tissue, to provide emanating light;
- d.) collecting the emanating light; and
- e.) evaluating the emanating light to determine whether the target tissue exhibits one or more characteristics indicating that the target tissue be biopsied.

31. A method for determining the orientation of an optical probe relative to a target tissue, the method comprising:

- a.) placing the opposed jaws of the catheter of claim 3 or 13 adjacent to a target tissue *in vivo*;
- b.) extending the optical probe and opening the jaws of the catheter;
- c.) emitting light from the at least one illumination light guide to the target tissue under conditions suitable to cause light to emanate from the target tissue, to provide emanating light;
- d.) collecting the emanating light entering the at least three collection light guides;
- e.) measuring the relative intensity of the light collected by each of the at least three collection light guides; and

f.) therefrom determining an orientation of the optical probe with respect to the target tissue.

32. A method for determining the orientation of an optical probe relative to a target tissue, the method comprising:

- a.) placing the opposed jaws of the catheter of claim 4 or 14 adjacent to a target tissue *in vivo*;
- b.) extending the optical probe and opening the jaws of the catheter;
- c.) emitting light from each of the at least three illumination light guides to the target tissue under conditions to cause light to emanate from the target tissue, to provide emanating light;
- d.) collecting the emanating light entering the at least three collection light guides;
- e.) measuring the relative intensity of the light collected by each of the at least three collection light guides; and
- f.) therefrom determining an orientation of the optical probe with respect to the target tissue.

33. The method of claim 30 wherein the extending of the optical probe forces apart the opposed jaws.

34. The method of claim 31 wherein the extending of the optical probe forces apart the opposed jaws.

35. The method of claim 32 wherein the extending of the optical probe forces apart the opposed jaws.

36. The method of claim 31 wherein the method further comprises, after determining the orientation of the optical probe, determining whether the orientation of the

optical probe is adequate to provide data sufficient to indicate that the target tissue exhibits one or more characteristics indicating that the target tissue be biopsied.

37. The method of claim 32 wherein the method further comprises, after determining the orientation of the optical probe, determining whether the orientation of the optical probe is adequate to provide data sufficient to indicate that the target tissue exhibits one or more characteristics indicating that the target tissue be biopsied.

38. The method of claim 30 wherein the method further comprises obtaining the biopsy by retracting the optical probe and closing the jaws of the catheter, thereby removing a piece of the target tissue from the target tissue.

39. The method of claim 31 wherein the method further comprises obtaining the biopsy by retracting the optical probe and closing the jaws of the catheter, thereby removing a piece of the target tissue from the target tissue.

40. The method of claim 32 wherein the method further comprises obtaining the biopsy by retracting the optical probe and closing the jaws of the catheter, thereby removing a piece of the target tissue from the target tissue.

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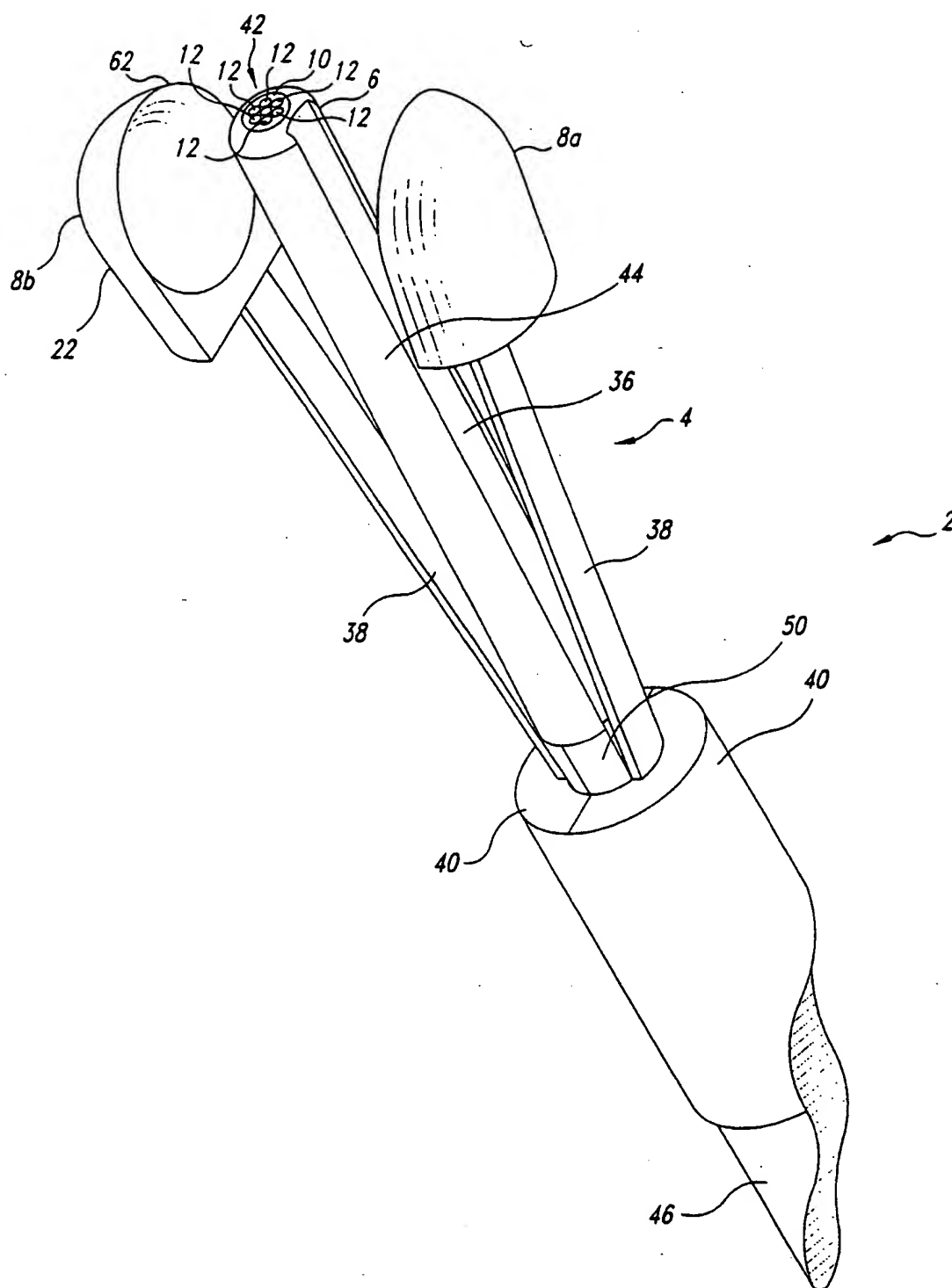
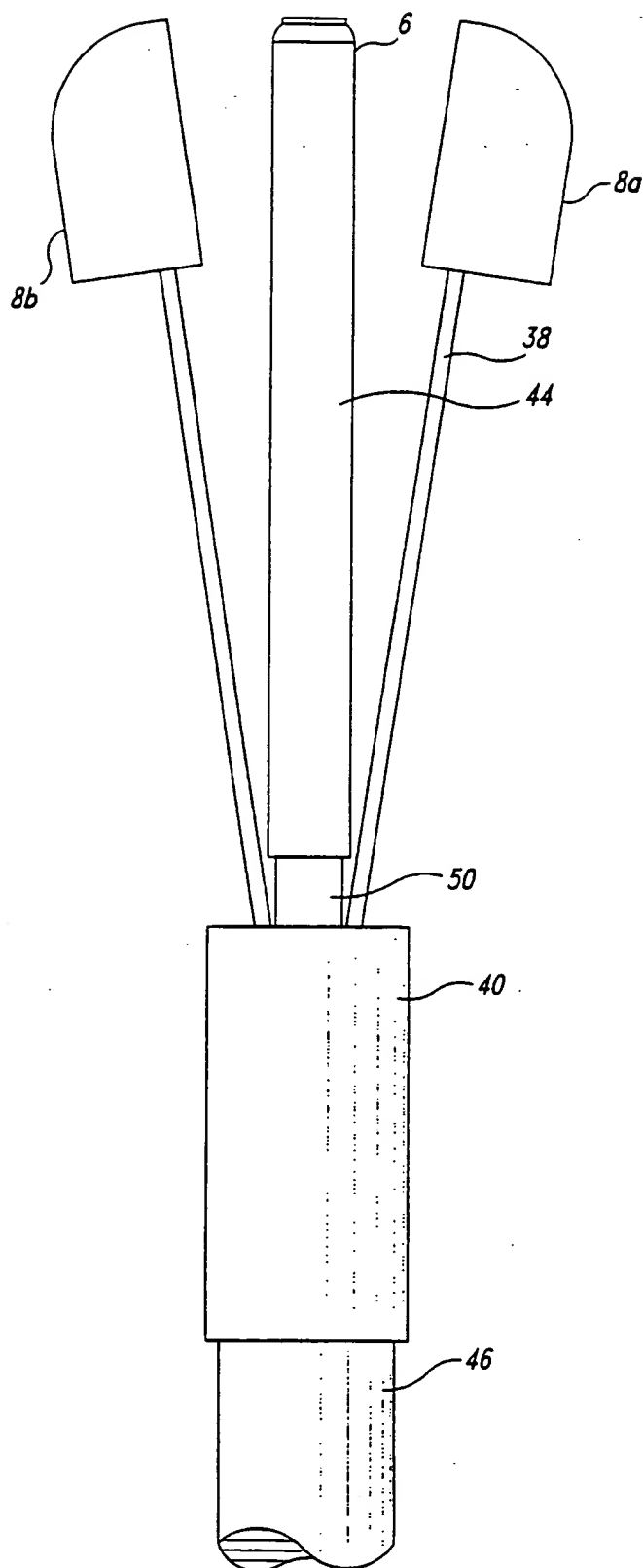


Fig. 1

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*Fig. 2*

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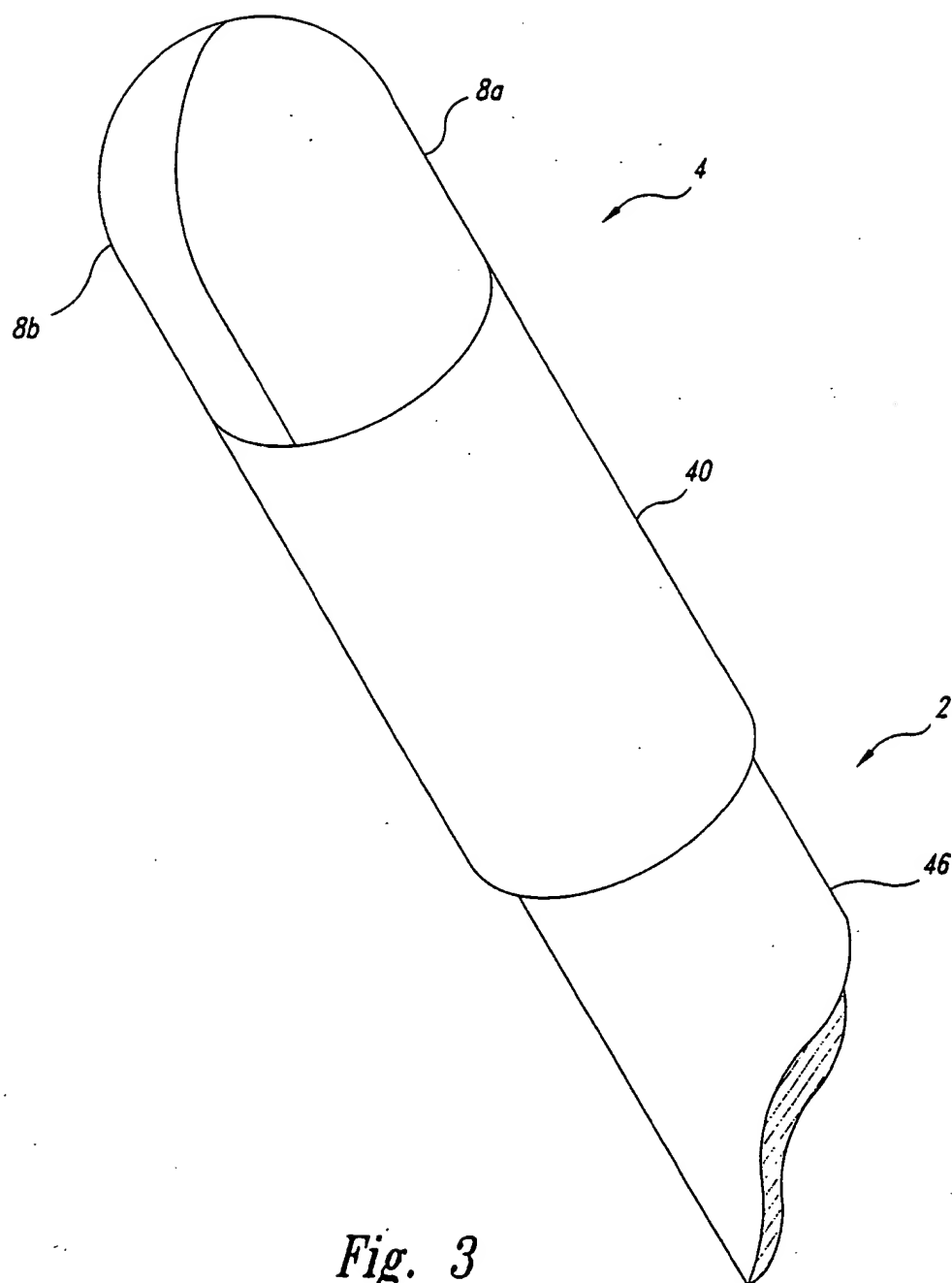


Fig. 3

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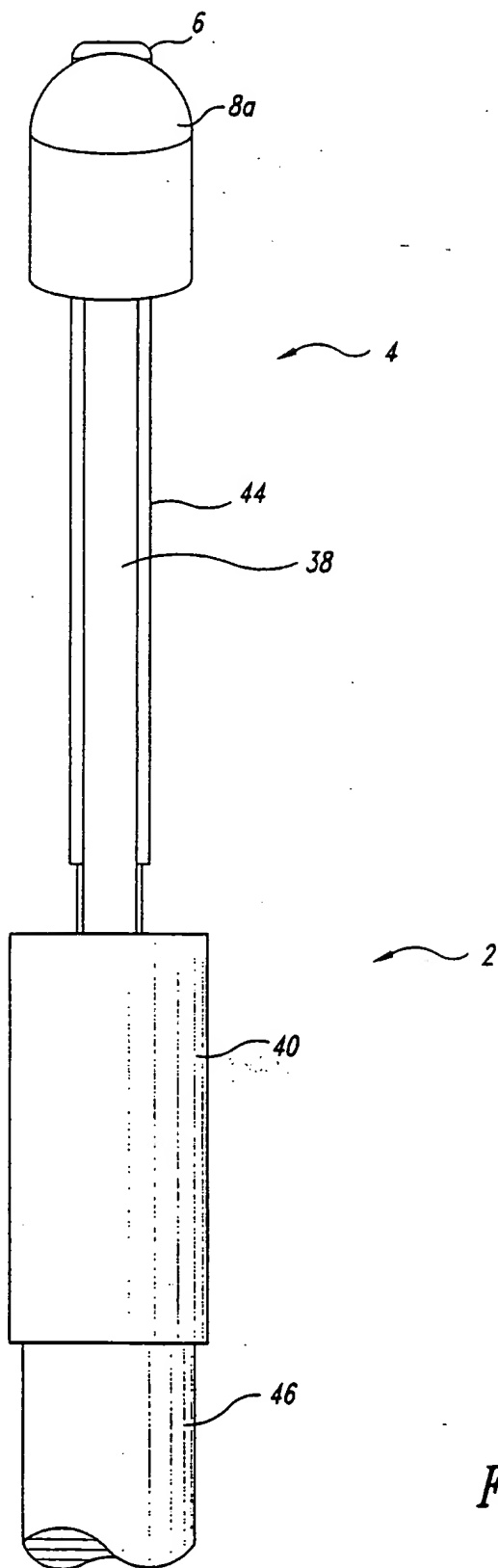
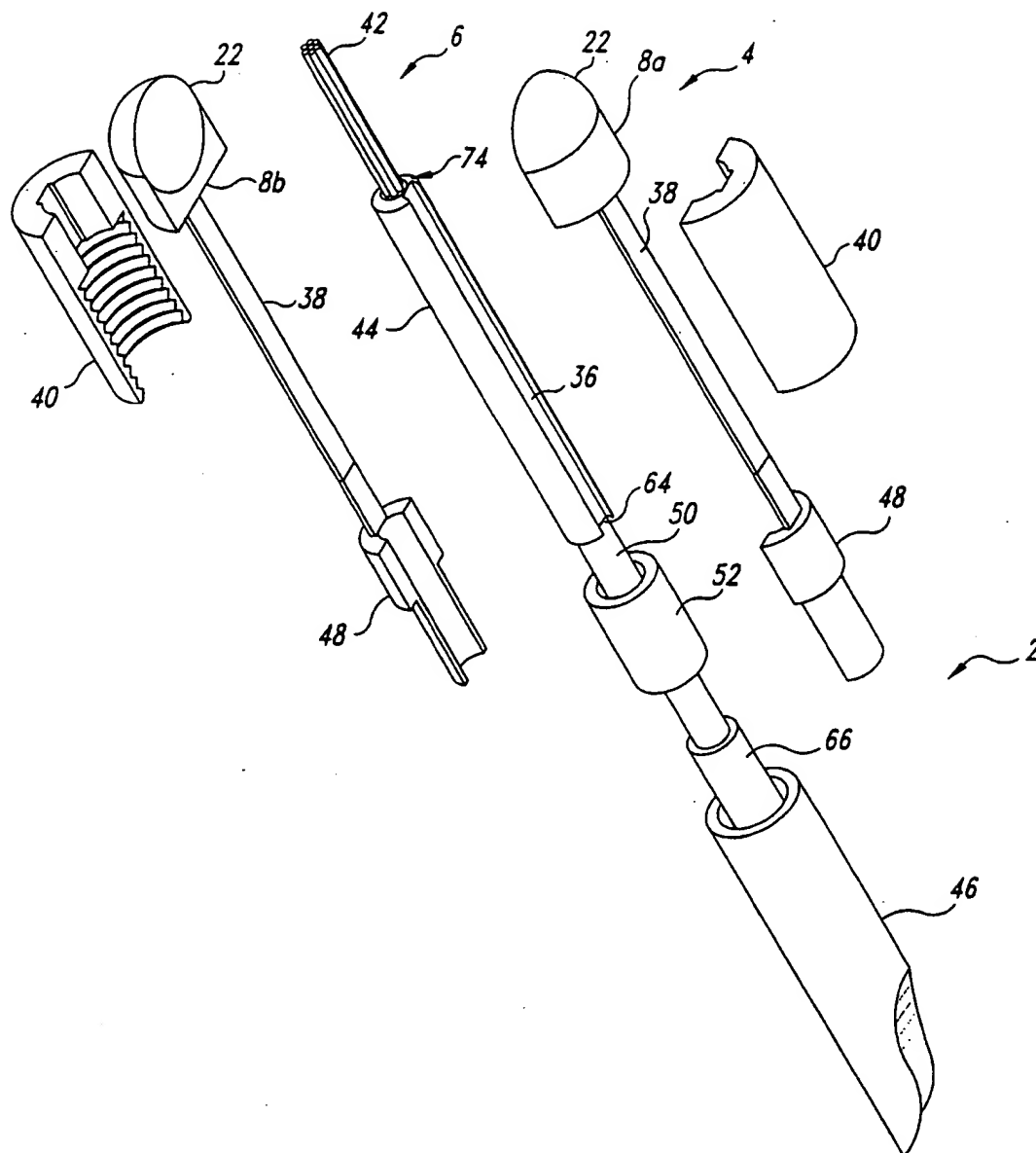


Fig. 4

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*Fig. 5*

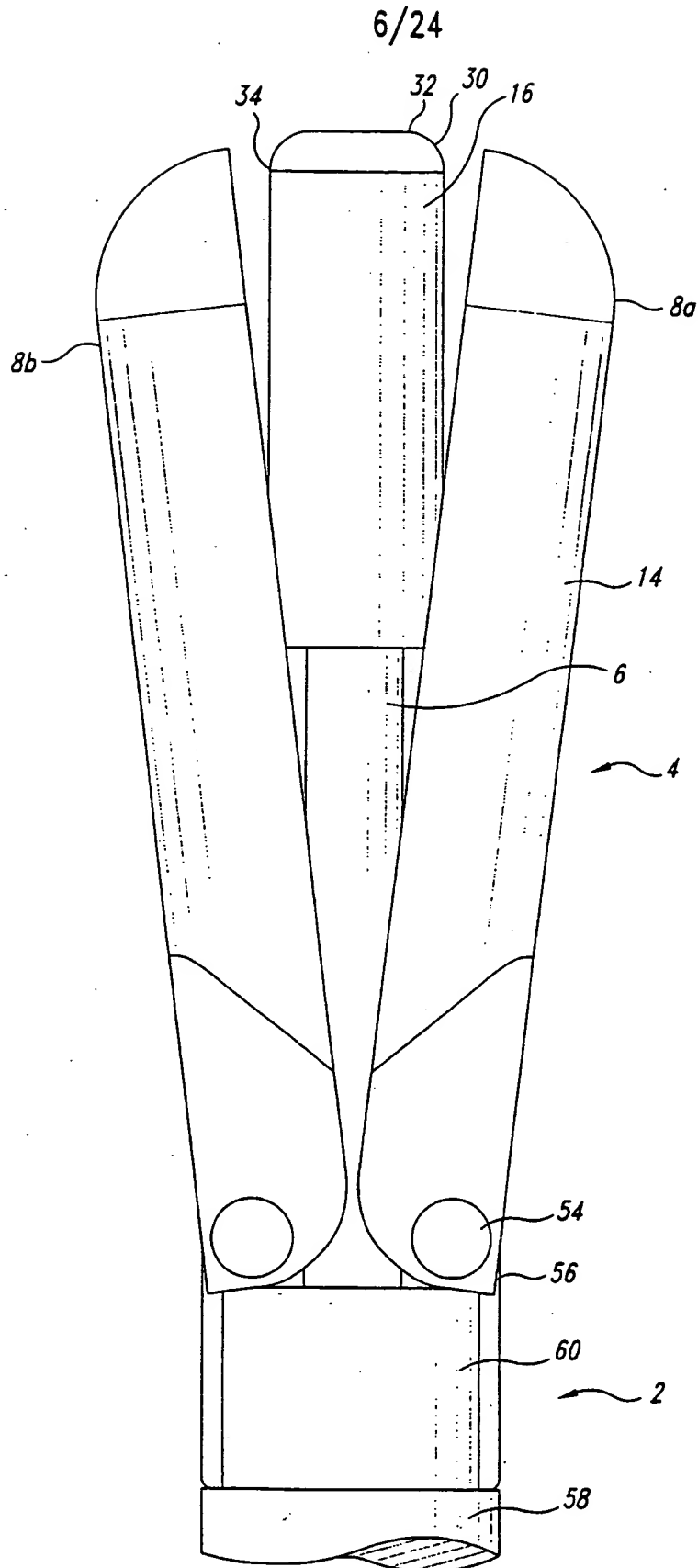
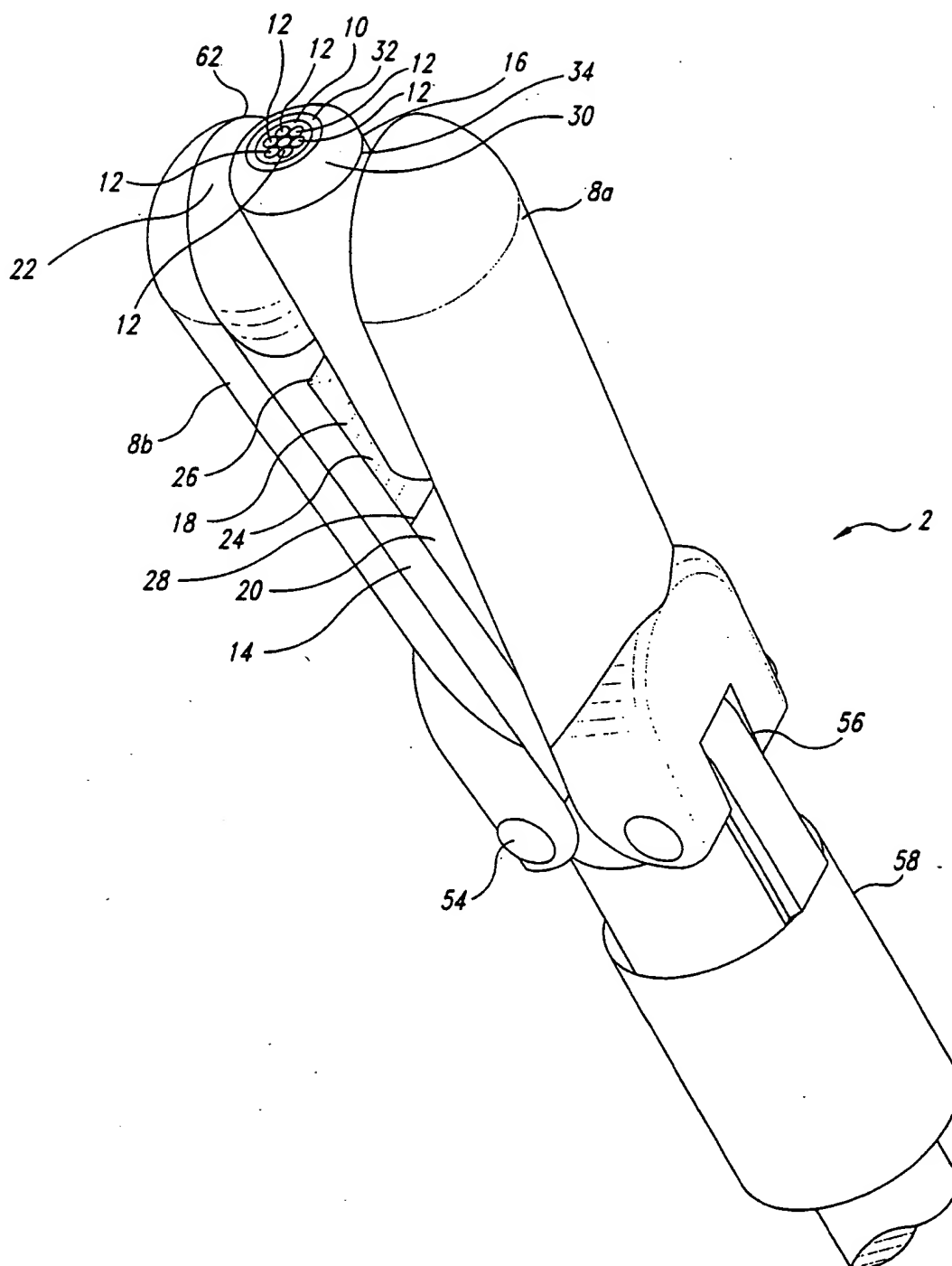
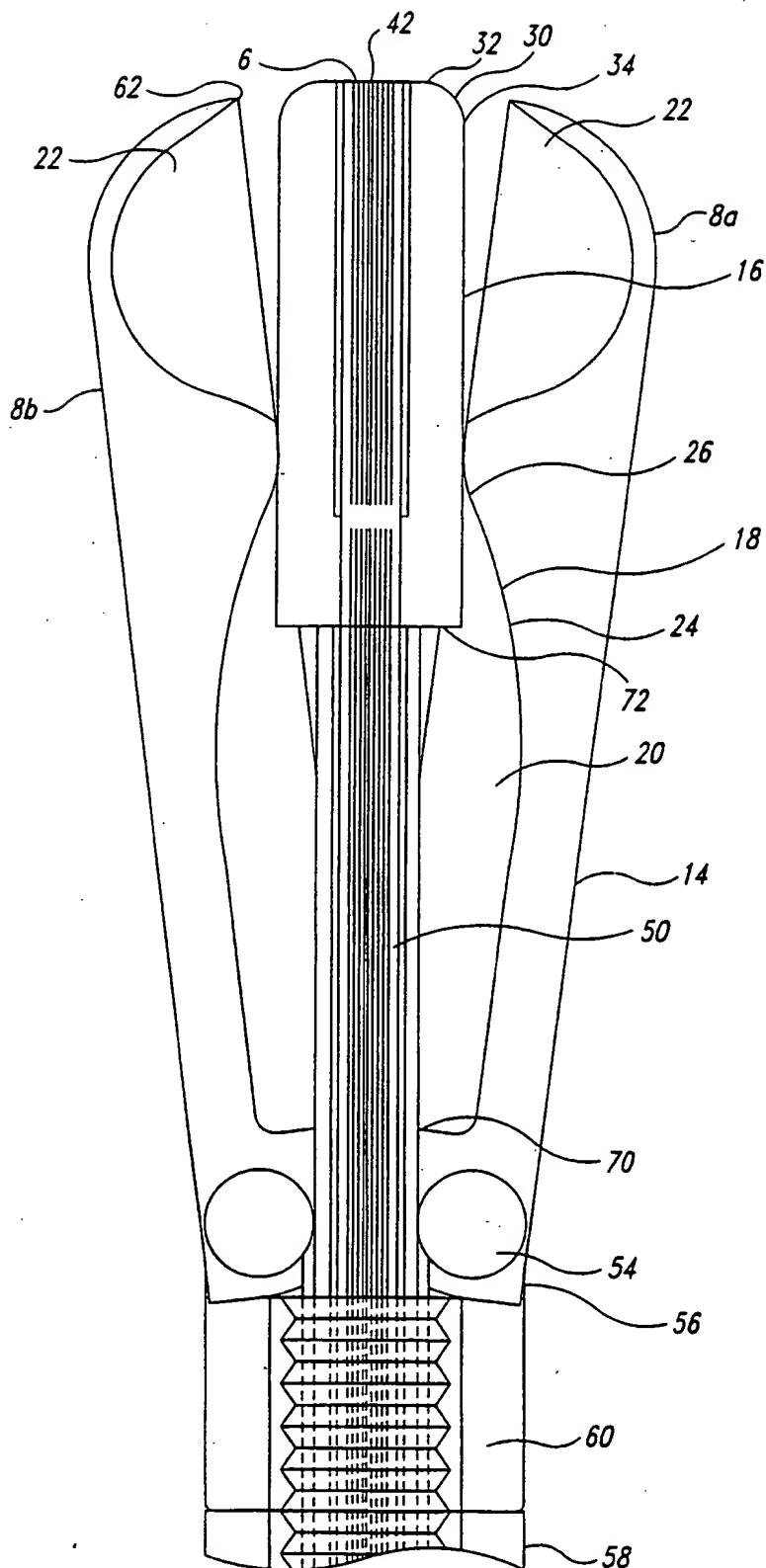


Fig. 6.

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*Fig. 7*

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*Fig. 8*

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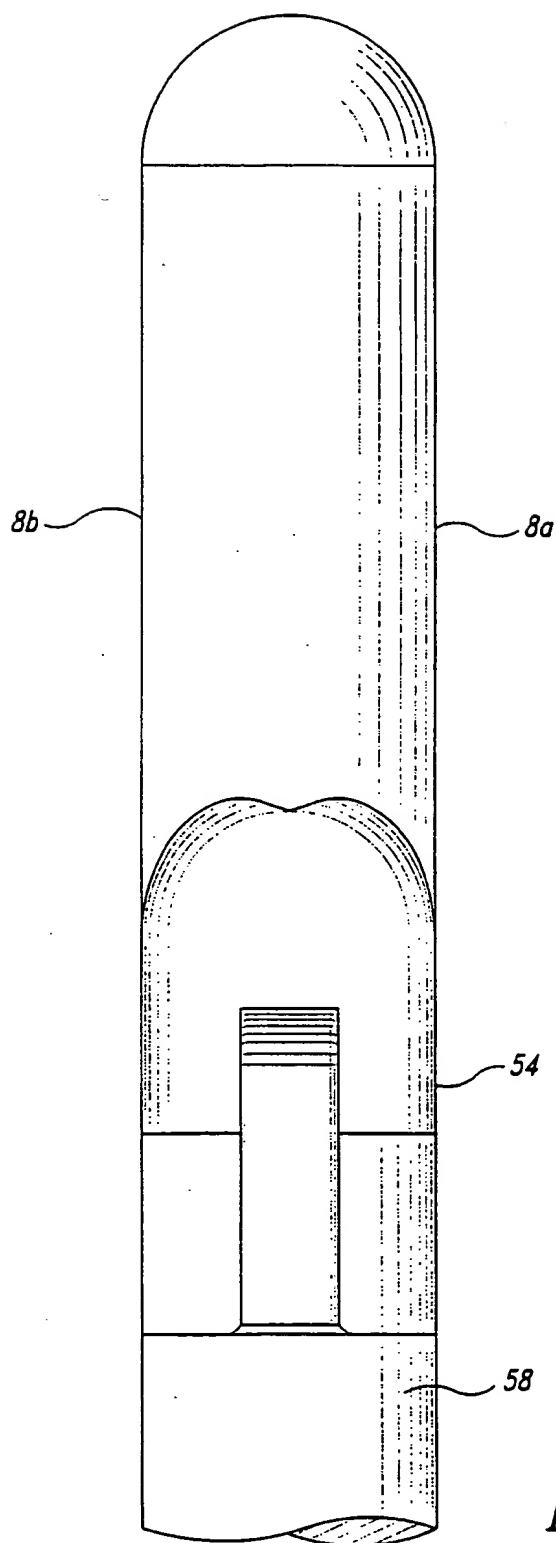


Fig. 9

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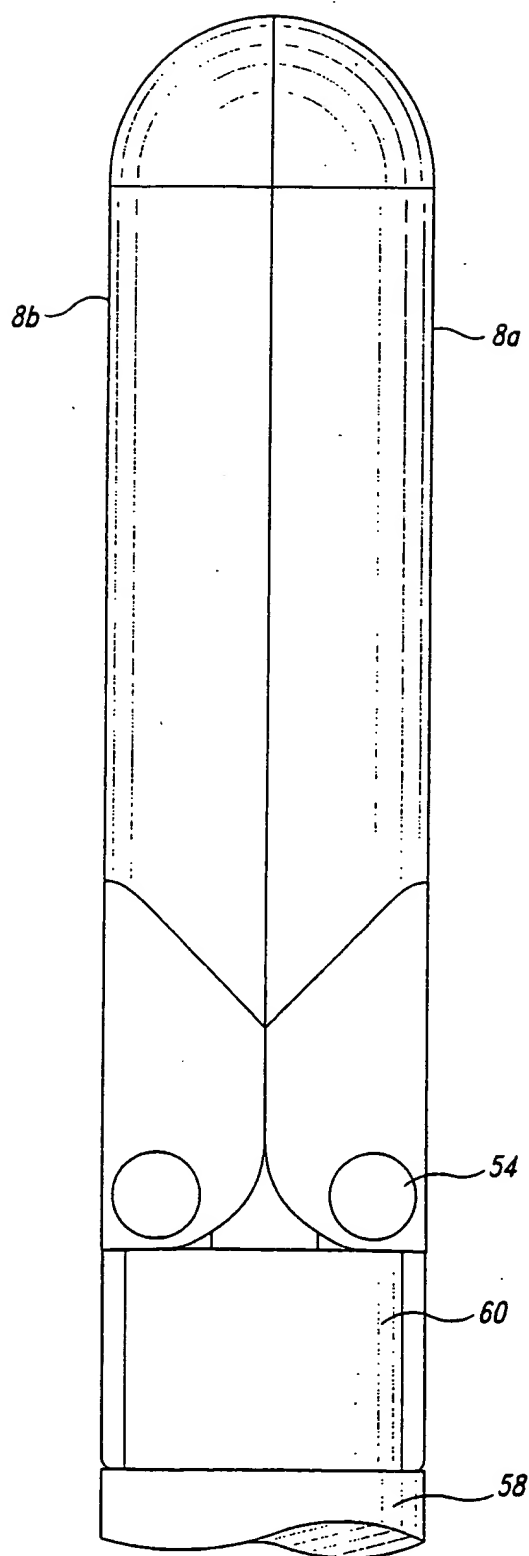


Fig. 10

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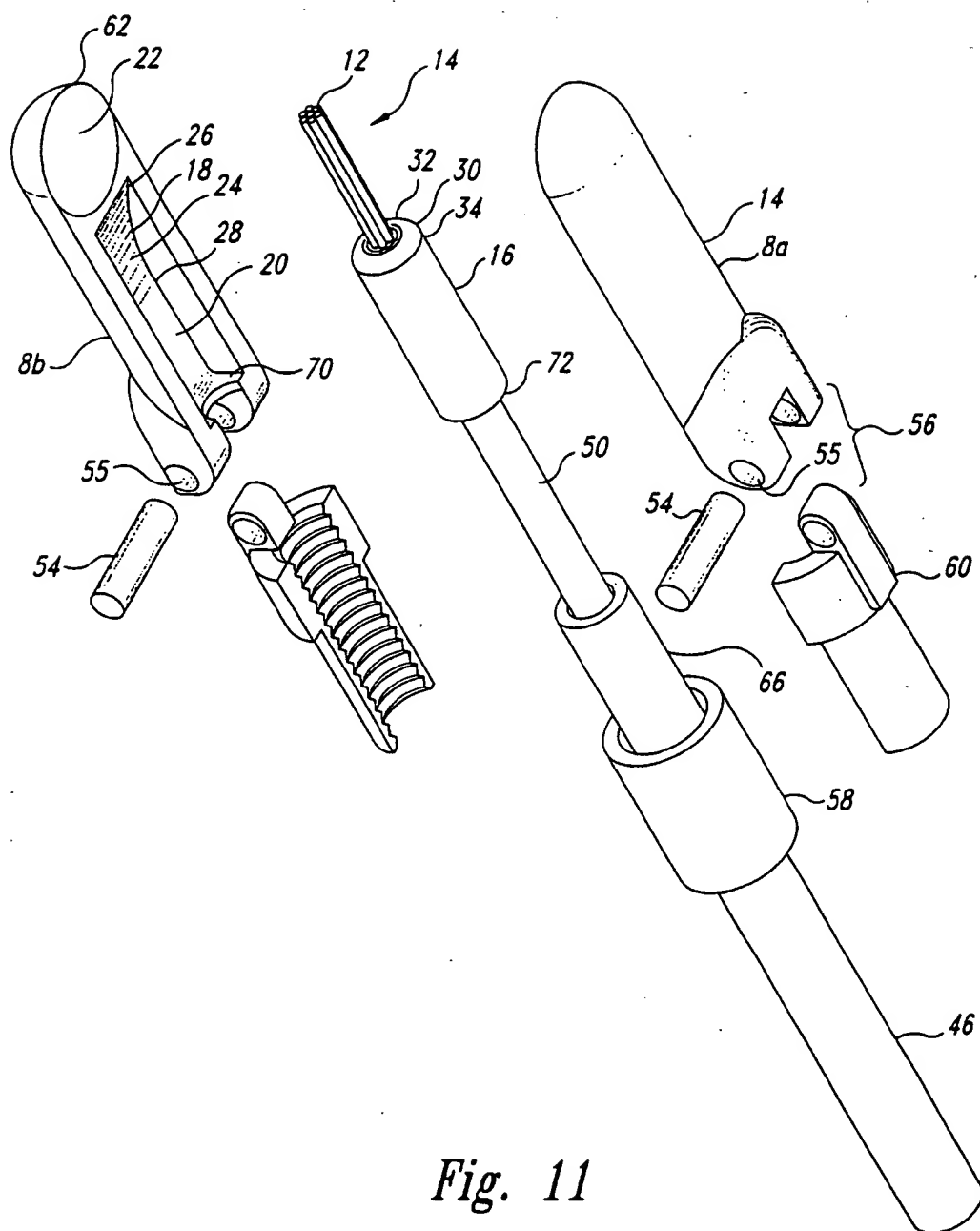


Fig. 11

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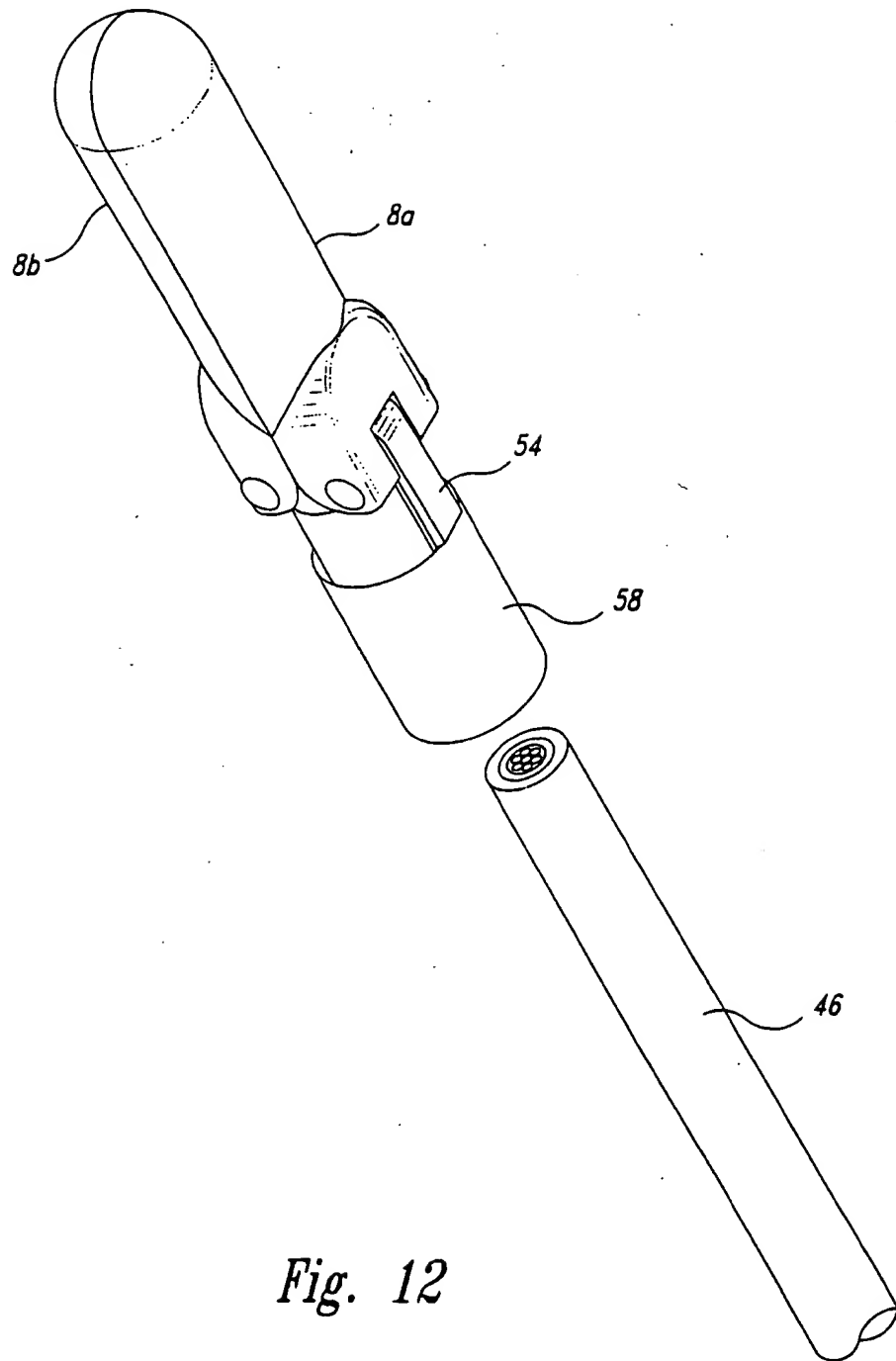
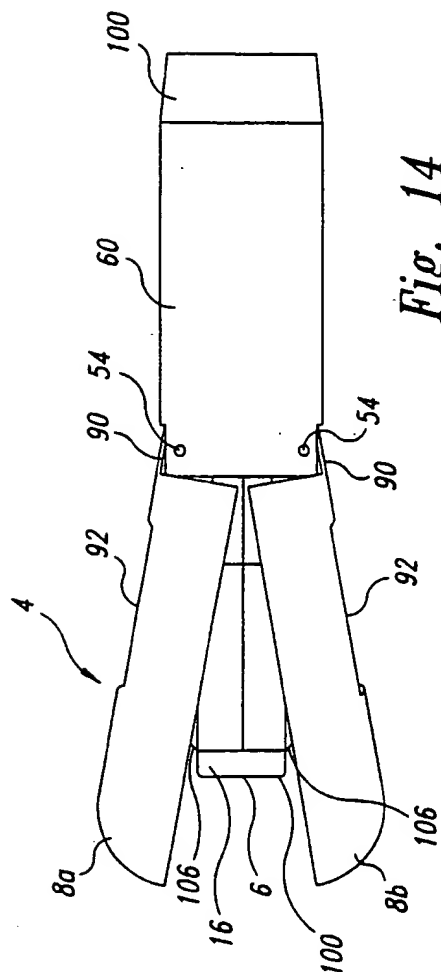
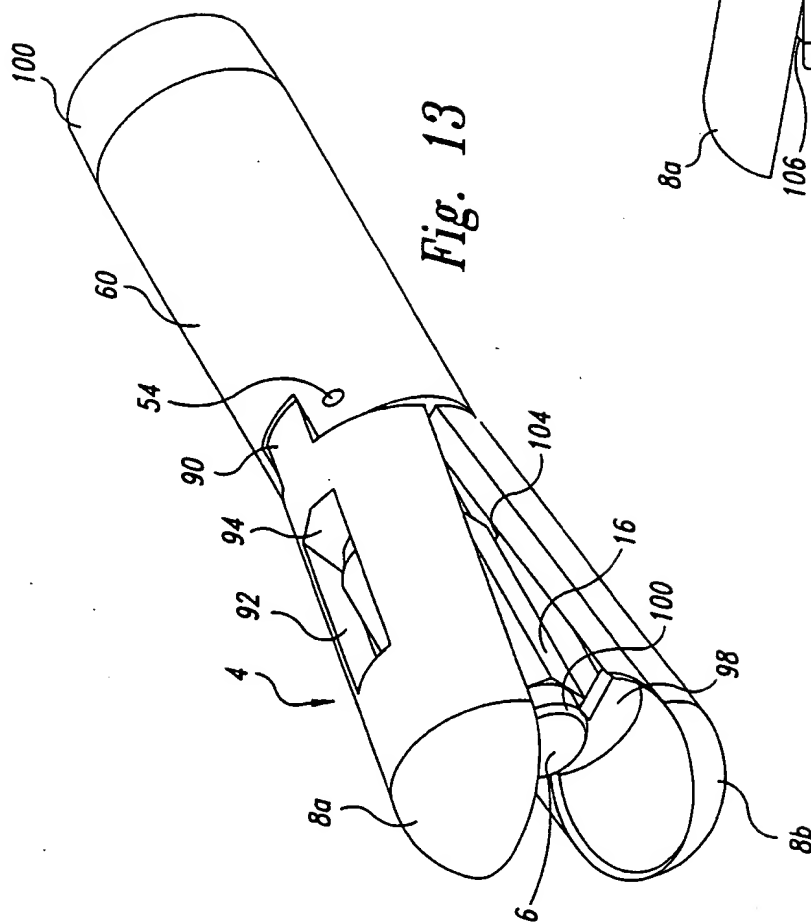


Fig. 12

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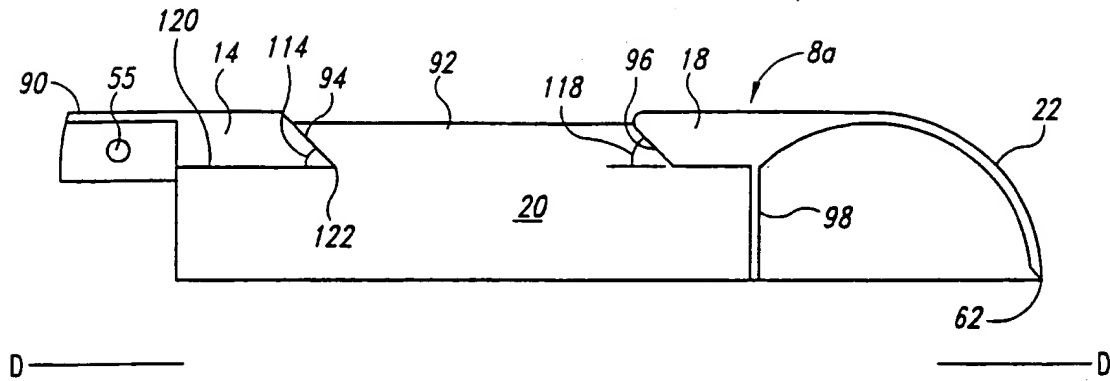


Fig. 15

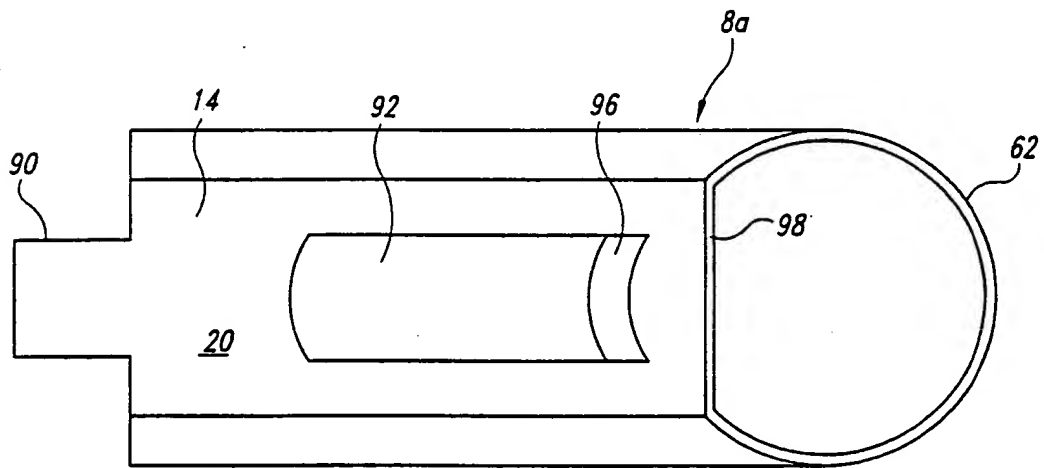


Fig. 16

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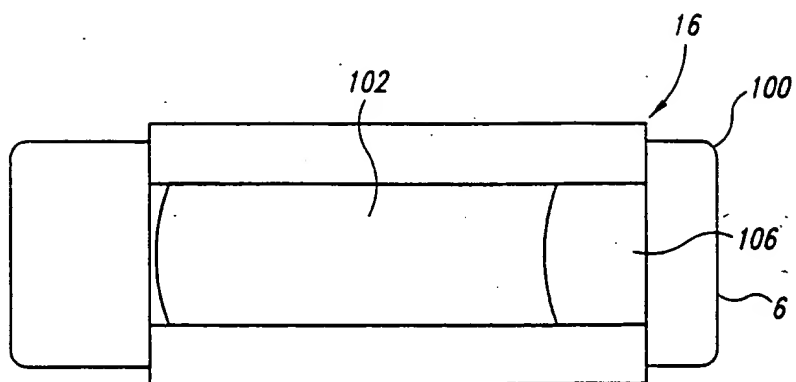


Fig. 17

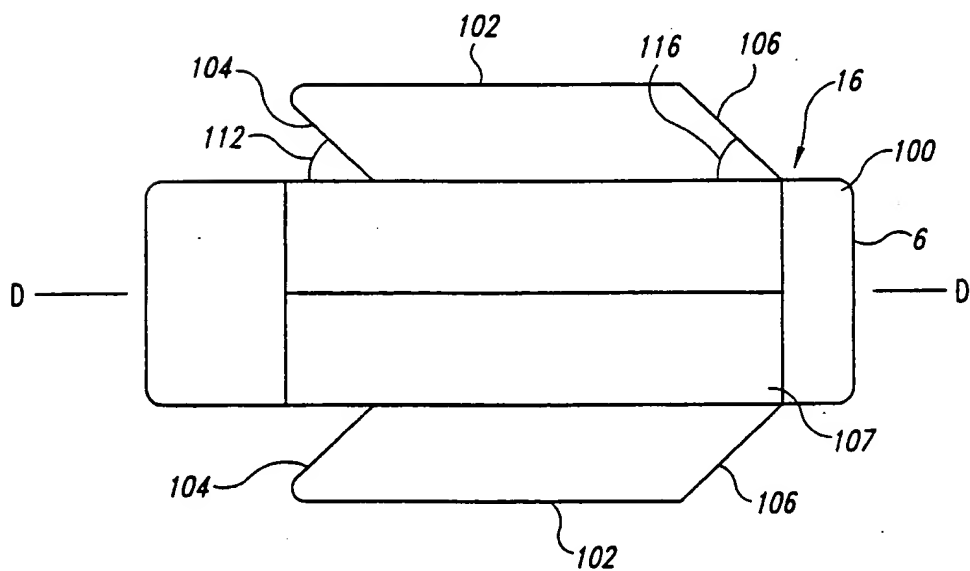


Fig. 18

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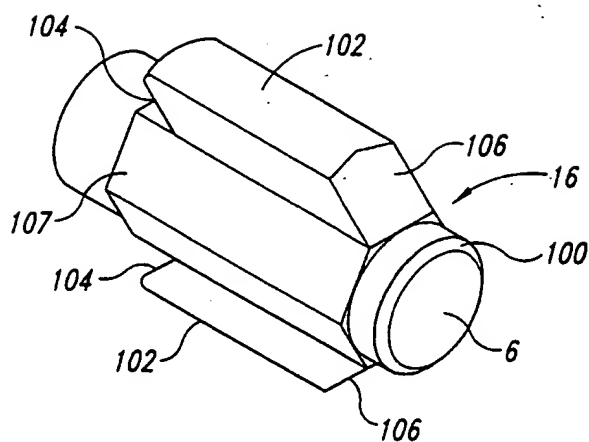


Fig. 19

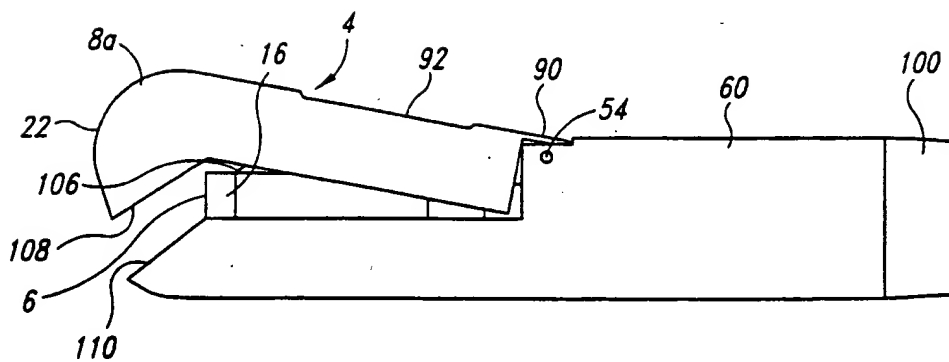


Fig. 20

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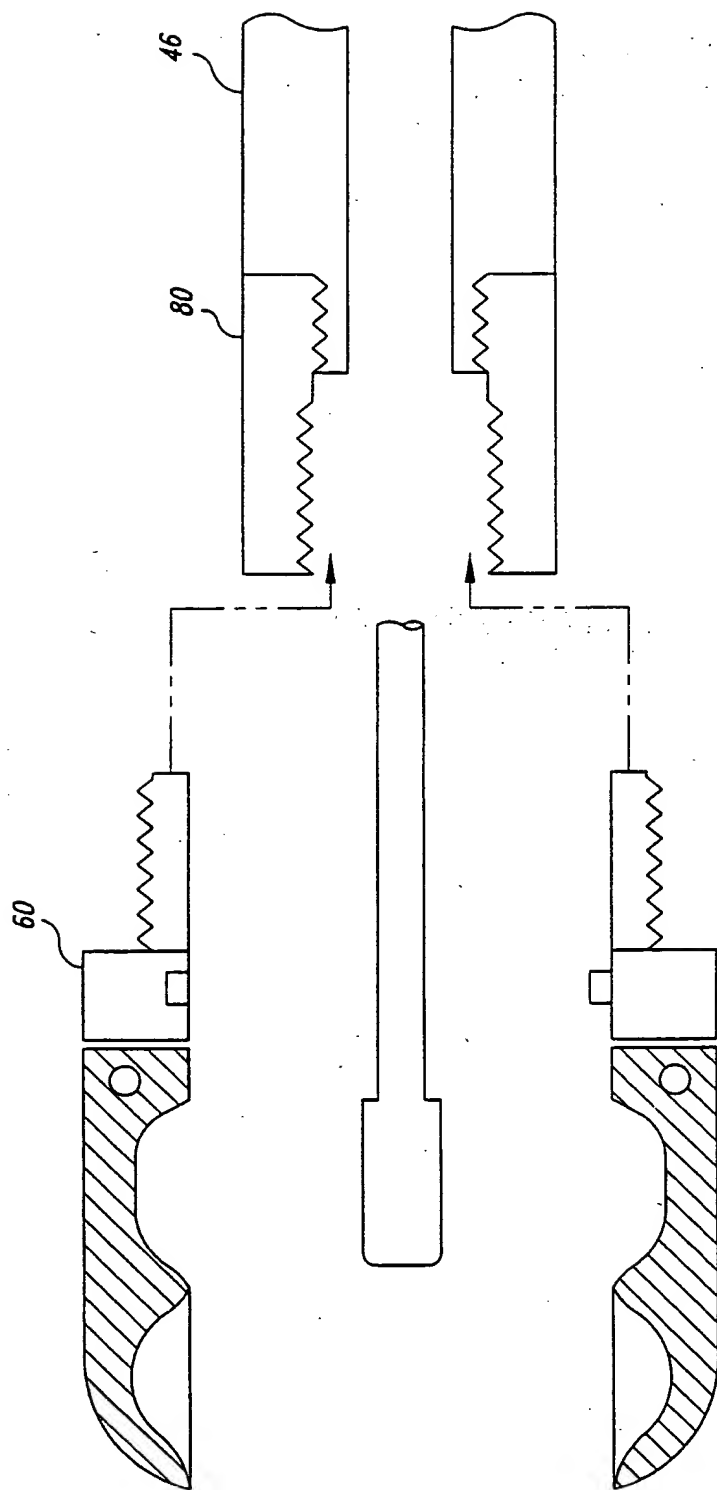


Fig. 21

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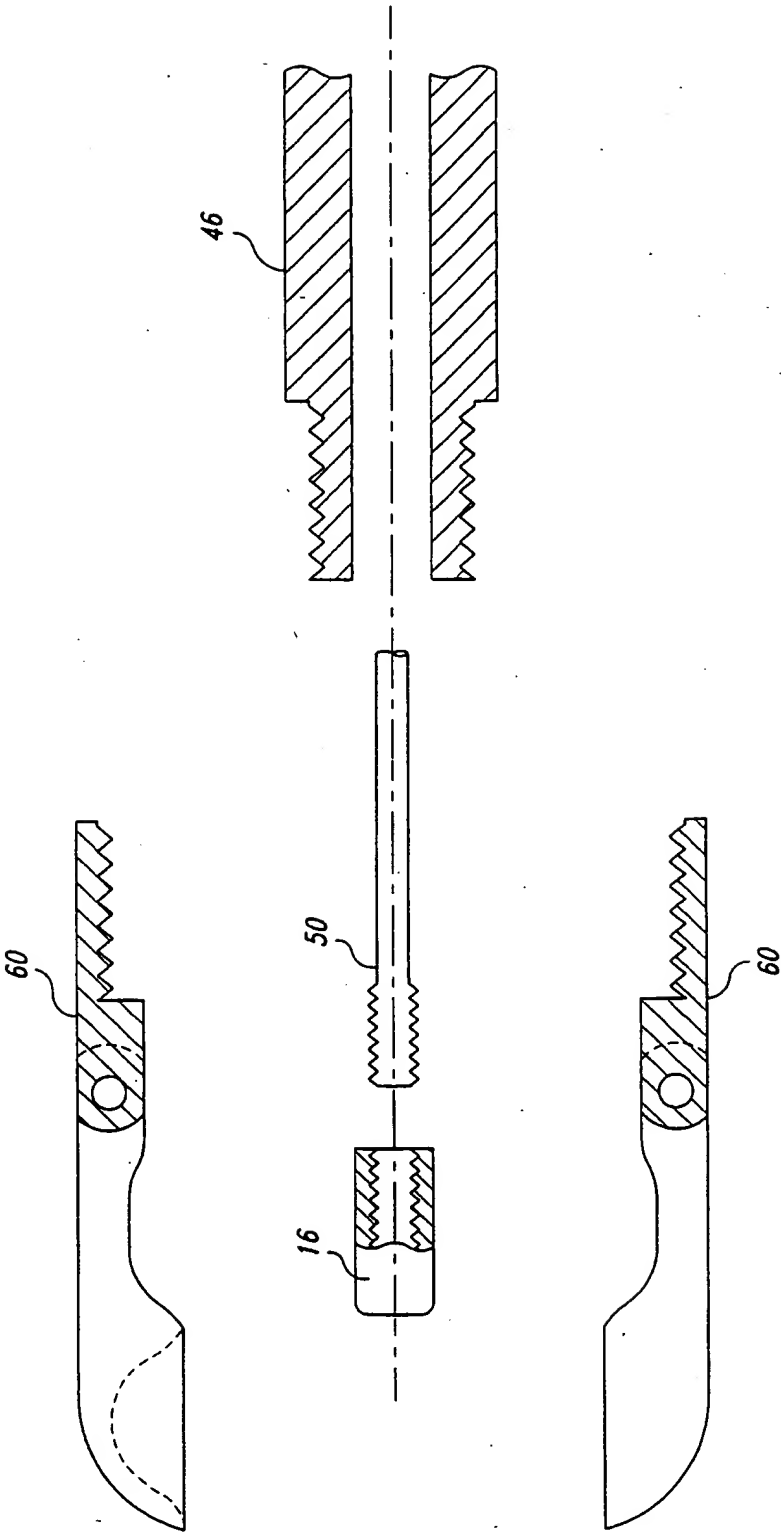
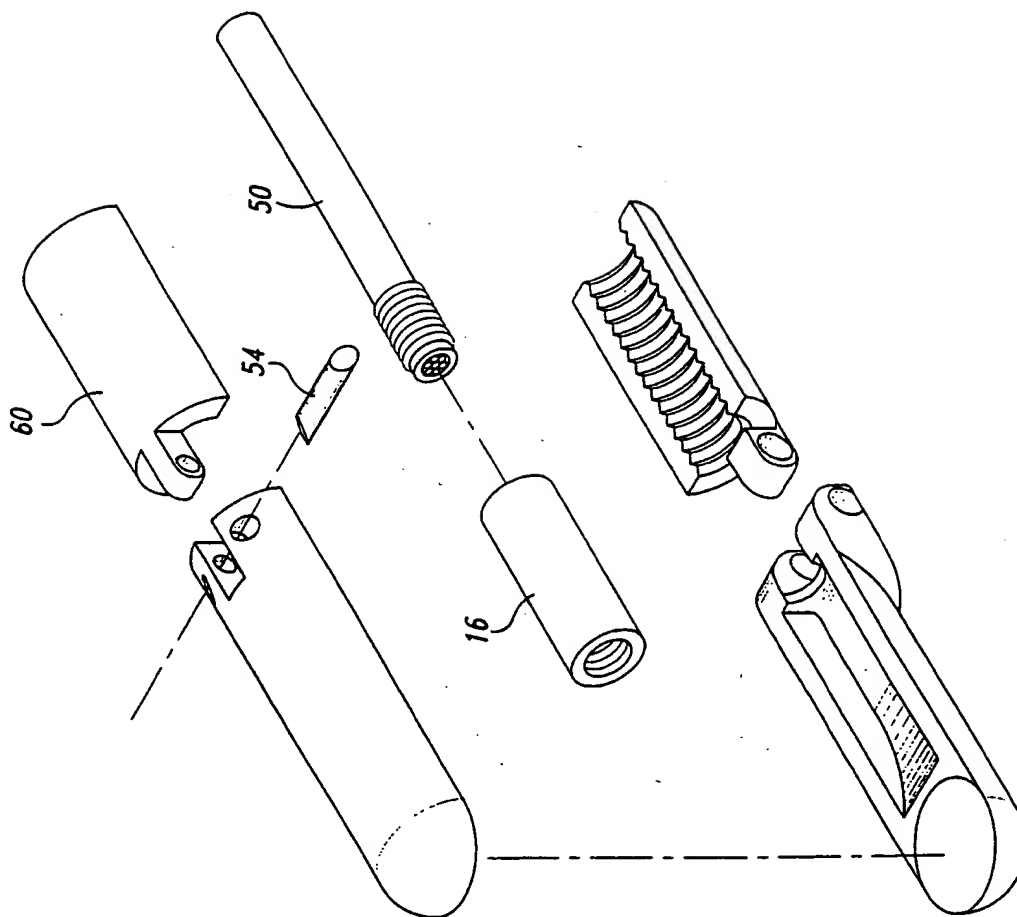


Fig. 22

Fig. 23



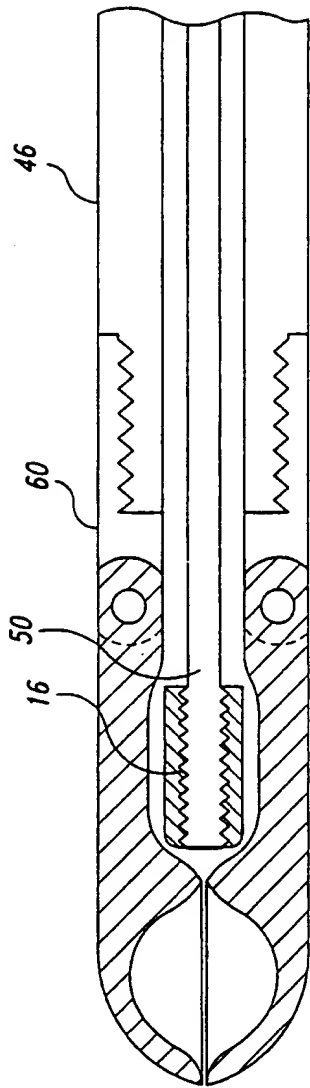


Fig. 24

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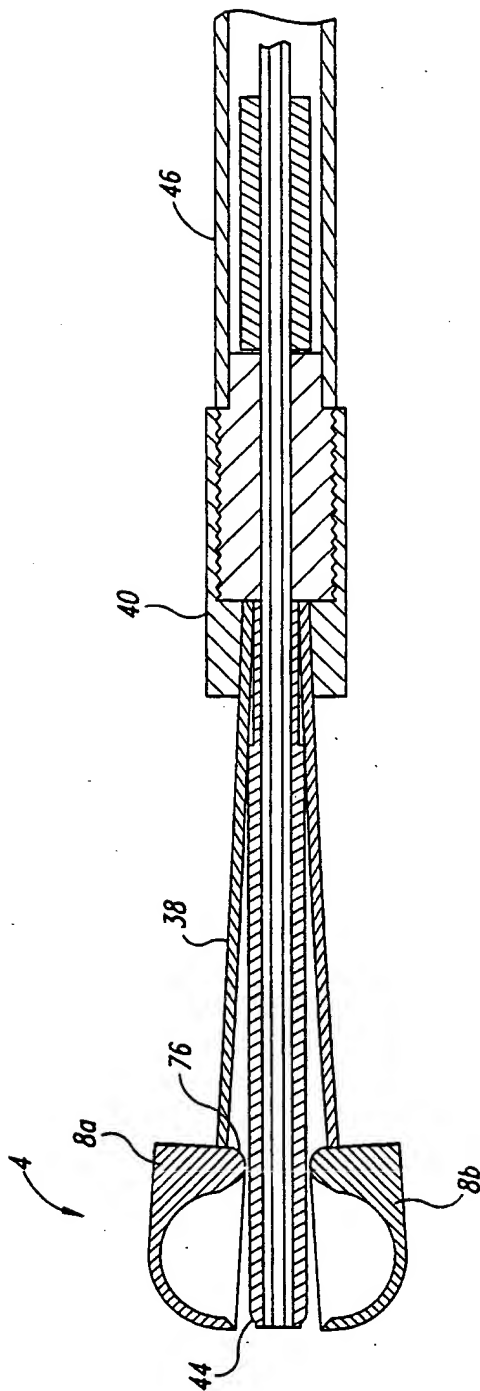


Fig. 25

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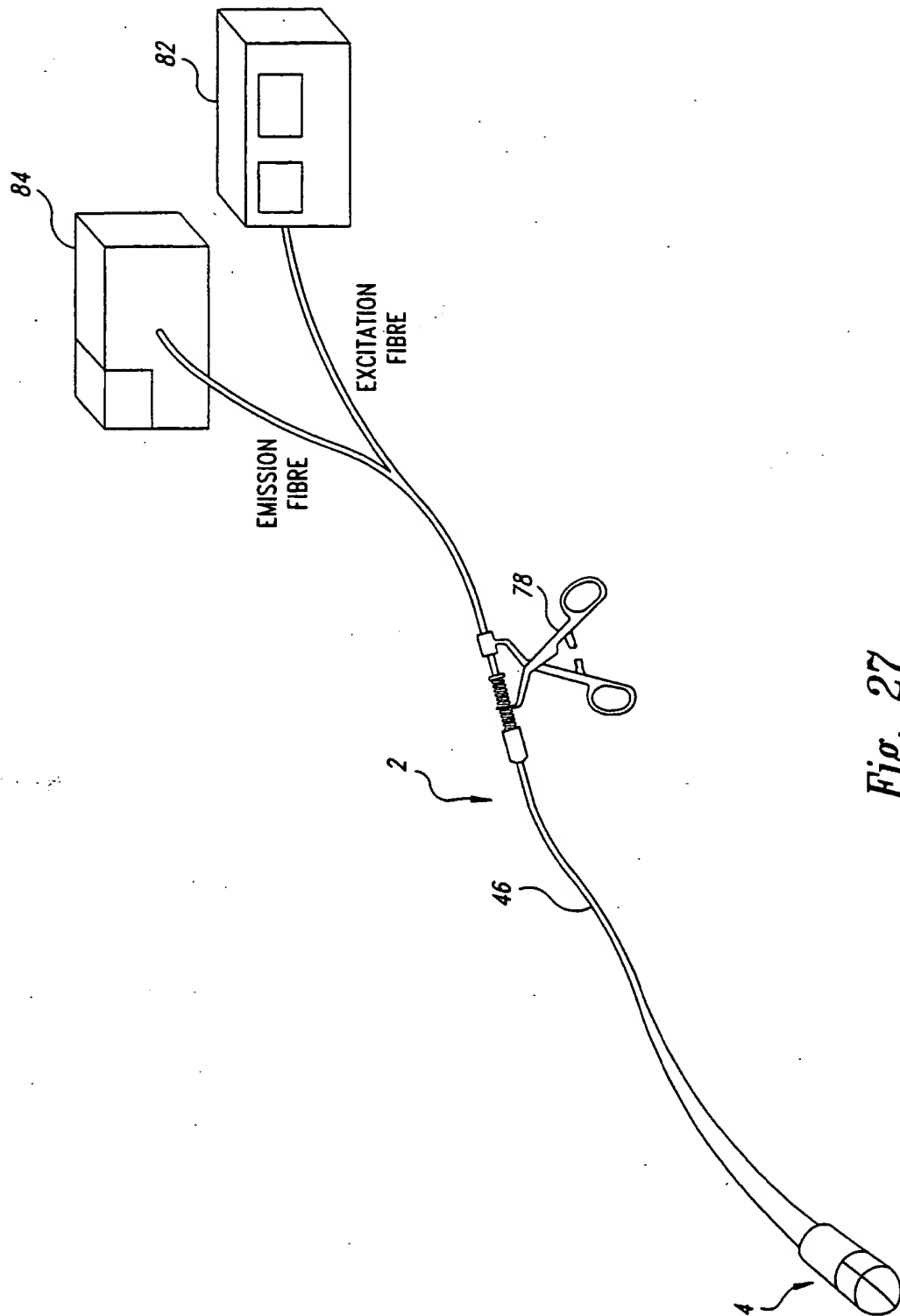


Fig. 27

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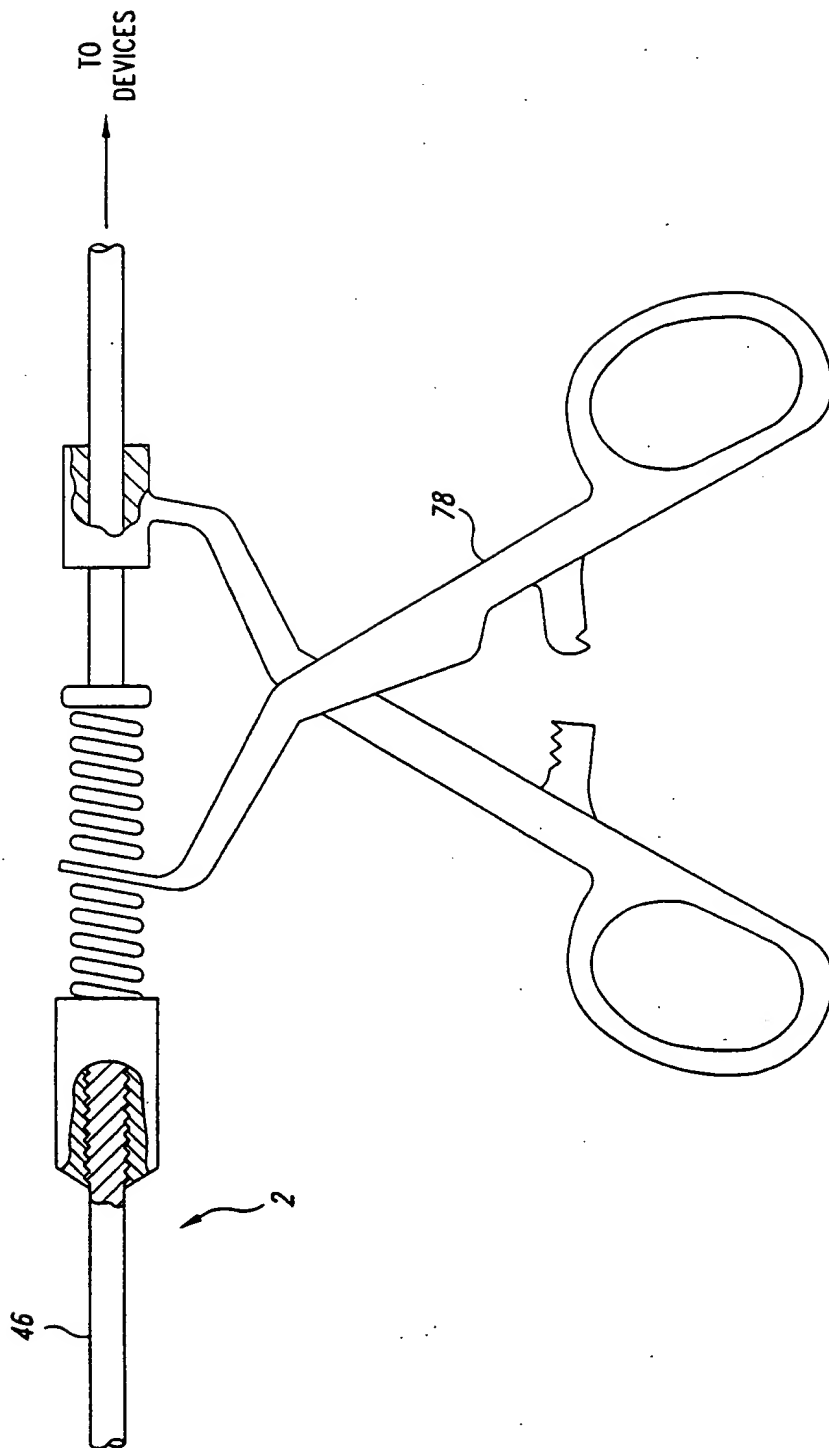


Fig. 28



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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<p>(21) International Application Number: PCT/CA98/00191 (22) International Filing Date: 12 March 1998 (12.03.98) (30) Priority Data: 60/040,557 13 March 1997 (13.03.97) US 60/046,368 15 May 1997 (15.05.97) US 60/053,688 25 July 1997 (25.07.97) US (71) Applicant: BIOMAX TECHNOLOGIES, INC. [CA/CA]; 568 - 999 Canada Place, Vancouver, British Columbia V6C 3E1 (CA). (72) Inventors: WHITEHEAD, Peter, D.; 2440 Queens Avenue, West Vancouver, British Columbia V7V 2Y6 (CA). MacAULAY, Calum, E.; 338 West 37th, Vancouver, British Columbia V5W 1E7 (CA). MacKINNON, Nicholas, B.; 2438 West Broadway, Vancouver, British Columbia V6K 2E7 (CA). ZENG, Haishan; 11786 - 85B Avenue, Delta, British Columbia V4C 2W2 (CA). (74) Agents: NASSIF, Omar, A. et al.; Gowling, Strathy & Henderson, Suite 4900, Commerce Court West, Toronto, Ontario M5L 1J3 (CA).</p>		<p>(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG). Published <i>With international search report.</i> <i>Before the expiration of the time limit for amending the claims</i> <i>and to be republished in the event of the receipt of amendments.</i> (88) Date of publication of the international search report: 3 December 1998 (03.12.98)</p>
<p>(54) Title: CATHETERS AND ENDOSCOPES COMPRISING OPTICAL PROBES AND BIOPTOMES AND METHODS OF USING THE SAME</p> <p>(57) Abstract</p> <p>Apparatus and methods relating to an optical bioptome disposed at the distal end of a catheter or endoscope. The optical bioptome comprises an optical probe that is preferably extensible and retractable axially along the length of the catheter or endoscope, and the jaws of the optical bioptome are opened when the optical probe is extended and the jaws are closed when the optical probe is retracted.</p>		

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INTERNATIONAL SEARCH REPORT

Int. Patent Application No.

PCT/CA 98/00191

A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 A61B5/00 A61B10/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 A61B

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	DE 39 20 706 A (FOERSTER ERNST :DOMSCHKE WOLFRAM (DE)) 10 January 1991 see abstract ---	1, 5, 15, 16, 22, 26, 30-32
A	US 4 573 450 A (ARAKAWA SATOSHI) 4 March 1986 see abstract ---	1, 5, 15, 16, 22, 26, 30-32
P, X A	WO 97 41776 A (SPECTRASCIENCE INC) 13 November 1997 see claims 1-14; figures 1-8 see page 2, line 11 - page 4, line 16 ---	1-30, 33, 38 31, 32, 34-37, 39, 40

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Date of the actual completion of the international search

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INTERNATIONAL SEARCH REPORT

International Application No

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5 452 723 A (WU JUN ET AL) 26 September 1995 see abstract ---	1, 5, 15, 16, 22, 26, 30-32
A	US 5 421 339 A (RAMANUJAM NIRMALA ET AL) 6 June 1995 see abstract -----	1, 5, 15, 16, 22, 26, 30-32

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/CA 98/00191

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
DE 3920706 A	10-01-1991	NONE	
US 4573450 A	04-03-1986	JP 60104915 A DE 3441029 A	10-06-1985 23-05-1985
WO 9741776 A	13-11-1997	US 5762613 A	09-06-1998
US 5452723 A	26-09-1995	NONE	
US 5421339 A	06-06-1995	AU 6946894 A CA 2162922 A EP 0702526 A JP 8511179 T WO 9426168 A US 5623932 A	12-12-1994 24-11-1994 27-03-1996 26-11-1996 24-11-1994 29-04-1997